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Ectopic Pregnancy*

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I WISH in the first place to express my deep appreciation of the great honour Professor James Young conferred upon me by inviting me to deliver two lectures at the Hammersmith British Postgraduate Medical School.

I have chosen for the first lecture the subject of ectopic pregnancy. This anomalous pregnancy is much more common than we suppose. Besides the cases which are definitely diagnosed as ectopic preganancy, many others are wrongly diagnosed as abdominal colic or appendicitis, and, treated as such, either die or recover spontaneously.

The prevalence of ectopic pregnancy as compared with intra-uterine has been estimated by Schümann[1] as 1 in 200. Farrar[2] found the ratio as compared with other gynaecological conditions to be 1.5 per cent. According to Wynne[3] it is 1.3 per cent.

The term ectopic gestation was originally coined by Robert Barnes and is a more widely inclusive term than "extra-uterine gestation". It covers conditions in which gestation may be ectopic without being extra-uterine, such as an interstitial pregnancy, pregnancy in a rudimentary horn of a bicornute uterus;

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and also those rare conditions described by Döderlein and Herzog[4] in which pregnancy occurred in an adenomyomatous uterus in crypts deep to its cavity.

The first mention of this anomalous pregnancy was made by Albucassis (Abou El-Kassim El-Zahrawi), the well-known Andalusian Arab surgeon (1013–1106) in his book *Al Tasrif*.[5] In the case he described, the gestation-sac had suppurated and the abscess perforated through the abdominal wall.

His description runs as follows:—

> I have come across a woman who conceived, and the foetus died in her inside. She conceived a second time, and the second foetus also died. After a long interval of time this woman developed an abscess in her hypogastric region. This abscess burst and discharged lots of pus. I was asked to look after her. I dressed the abscess for a long time without success. I therefore applied to it ointments possessing strong powers of suction. Bones began to be discharged from the wound. I was surprised at this, as I know that the abdomen contains no bones. I therefore conceived the idea that these bones belonged to the dead foetus. I explored the cavity and removed many bones. The patient recovered and lived for a long time, enjoying perfect health, the abscess continuing to discharge a little pus.

According to Pierre A. Huet[6] ectopic pregnancy was well known in the eighteenth century. He tells us that this subject was mentioned in the *Theatrum Anatomicum* by Genevois Manget (1652–1742), in which excellent plates appear showing the lesions in the Fallopian tubes and ovaries. The cases include ovarian pregnancy, rupture with intraperitoneal bleeding, a case of tubal abortion without septic complications, a case of tubal pregnancy with infection of the sac and fistula formation, and, lastly, one of a lithopaedion.

Prior to 1838 ectopic pregnancy was often confused with rupture of the pregnant uterus. The papers of Velpeau[7] and Dezemièris,[8] published in 1836, made the difference between the two conditions quite clear. In 1842 William Campbell, a teacher of midwifery in Edinburgh, published an important work in which he collected all the material on this subject up to that time, and exhaustively investigated the literary history. In 1876 John S. Parry,[9] of Philadelphia, published a book on ectopic pregnancy, which is commented upon by Lawson Tait[10] as "at once remarkable for its scholarly research and fine critical sagacity."

Aetiology. There has been a great deal of speculation as regards the factors which lead to the arrest and development of the fertilized ovum outside the uterine cavity.

Fritze (1779), Virchow and Hecker[11] first drew attention to the fact that peritoneal adhesions might cause tubal pregnancy either by compressing the lumen of the Fallopian tube or by interference with its peristalsis.

In 1888 Lawson Tait[10a] advanced the theory that the desquamative salpingitis described by John Bland-Sutton and Johnstone was the main cause, the desquamation of the epithelium in these cases favouring implantation of the ovum at the desquamated spot.

These views have been severely criticized by Bland-Sutton,[12] Martin,[13] Veit,[14] Webster,[15] Paquy,[16] and Couvelaire,[17] who proved by careful histological examination that ectopic foetation occurs as often, if not more often, in a healthy as in a diseased or imperfectly developed Fallopian tube. In spite of this these views are still held in a modified way by many writers, more especially as clinical observation tends to lend them support. The subjects of ectopic foetation are rarely very young, are often sterile for years, and generally give a history of previous salpingitis. In a series of 120 cases of tubal pregnancy, of which 78 cases were operated on by me at Kasr-el-Aini and at the Coptic and Kitchener Memorial Hospitals, 22 by Professor Roy Dobbin and 20 by Professor Ahmed Shafeek Bey, 10 patients only were under 25 years of age, while 65 admitted being over 30. More than half the patients gave a history of previous salpingitis and sterility. In most of the operations we performed on these patients adhesions, not only on the pregnant side but on the opposite side as well, were present and gave rise to a certain amount of difficulty in liberating the pregnant Fallopian tubes.

Werth,[18] Williams[19] and Opitz[25] made another step forward when they explained the process of formation of culs-de-sac in inflamed Fallopian tubes, the epithelial cells becoming desquamated and adjacent plicae adhering to one another during the process of healing. Blind alleys are thus formed in which an impregnated ovum may accidentally be held.

Delay in the downward passage of the ovum has also been put forward as one of the causes. It may be brought about by stenosis of the lumen of the tube, by inefficiency of the peristaltic movements caused by kinks or adhesions, or by failure of the downward currents which take part in driving the ovum towards the uterus as a result of extensive desquamation of the epithelium. Fig. 1 presents additional evidence bearing on this theory.

It is a case of interstitial foetation in which peritoneal adhe-

sions produced 2 distinct kinks in the wall of the tube. These kinks must have caused a certain amount of delay in the passage of the ovum. By the time the ovum has overcome these obstacles it had either grown too large to pass through the narrow interstitial portion of the tube, or else its zona radiata was lost and the surrounding trophoblasts proliferated to an extent sufficient to enable them to bore their way and implant the ovum into the mucous membrane of the tube.

Some observers believe that interference with the passage of the ovum may in certain cases be caused by polypi projecting into the lumen of the Fallopian tube or may result from the pressure of tumours in the wall of the tube or in the adjacent organs. Fig. 2 illustrates the last point. It represents 1 of our cases in which a large parovarian cyst had so flattened the lumen of the tube as to block it completely.

A very rare cause of ectopic foetation is post-operative separation of the edges of the uterine wound of a previous Caesarean section. Four cases of this kind, in which primary abdominal pregnancy occurred, are recorded by E. L. King.[21] In 3 of these the ovum had implanted itself in the omentum which filled the gap between the ununited uterine edges, while in the fourth case the ovum was implanted in the peritoneum of the anterior abdominal wall.

In spite of the extensive work which has been done in connexion with aetiology of ectopic pregnancy the question remains as great a problem to us as it was to our predecessors.

Pathological Anatomy.

Figs. 3 to 6 show the manner in which the ectopic ovum buries itself in the tubal tissues. Decidual reaction is scanty and incomplete. This fact affords the trophoblasts unresisted advance. The muscles and maternal veins are invaded for a long distance. According to Young[22] oedema and necrosis of the maternal tissues occur prior to their invasion by the foetal cells. He attributes this necrosis to the action of chemical substances secreted by the foetal cells.

Invasion of the maternal tissues leads to haemorrhage into the ovum and into the tubal muscle surrounding it. This may lead to intra-mural, intra-tubal (see Figs. 1 and 7), intra-peritoneal (Fig. 9), or extra-peritoneal haemorrhage (Fig. 10). The relative frequency of these terminations in our series was as follows:—

Ampullary and isthmial	96
Interstitial	4
Tubo-ovarian	3
Tubo-ligamentary	6
Tubo-abdominal (secondary abdominal)	4
Ovarian	1
Primary abdominal	1
In a rudimentary uterine horn	5
Total	120

Of this number, pregnancy advanced to the later months in 11 cases. In 3 of these pregnancy occurred in the ampullary portion of the tube and proceeded to term *without rupture*. In 3 more the foetus was converted into a lithopaedion inside the tube. In 1 patient an intraligamentary pregnancy went to term. In the 4 remaining patients secondary abdominal gestation occurred and the foetus developed till term. Out of the 11 patients only 1 came for treatment while the child was alive and viable.

Rupture into the peritoneal cavity occurred in about 58 per cent of the cases. It is well worth noting that in some cases in which rupture and intra-peritoneal haemorrhage occurred, the ovum had already been dead for some time and was converted into a fleshy mole. This is an additional proof, if one were needed, that the risk of rupture in tubal gestation does not cease with the death of the ovum.

Intra-tubal rupture with expulsion of the ovum into the peritoneal cavity occurred in 27 per cent. This number includes some cases in which expulsion from the tube was incomplete and a peri-tubal or a pelvic haematocele formed.

It will be noticed that we have completely discarded the term "tubal abortion" in favour of the less misleading and more exact term "intra-tubal rupture", adopted by Berkeley and Bonney.[23] These authors have suggested this term on account of the similarity they found between the process of rupture of the capsular membrane of the ovum into the lumen of the tube, a condition which always precedes expulsion of the ovum, and that of rupture of the wall of the pregnant tube into the peritoneum which leads to intra-peritoneal haemorrhage.

Rupture into the broad ligament occurred in 6 of our cases (5 per cent). In 2 of these the ovum died and a broad ligament haematoma was formed. In 4 cases the chorionic villi were not

much disturbed by the rupture and the ovum continued to develop inside the broad ligament. In 3 of these (Figs. 10A and 10B) the operation was performed while the child was alive but not viable. In the remaining case (Fig. 11) pregnancy continued till term without the occurrence of secondary rupture. False labour, followed by death of the foetus and expulsion of a decidual cast from the uterus, occurred before the patient applied for treatment. The ovum in this case has during its growth peeled the peritoneum off the psoas and iliacus muscles posteriorly, and off the abdominal wall anteriorly. The reflection which corresponds to the floor of the utero-vesical pouch has been displaced upwards to the level of the umbilicus. The ovary and its ligament are seen flattened on the wall of the sac. The extensive denudation of the pelvic organs brought the ovum into intimate relation with the rectum and bladder. The sac got infected and peritonitis occurred. As a result of this, peritoneal adhesions formed between the sac and the adjacent tissues. A big loop of gut adhered to the sac so densely that the adherent gut had to be resected before I was able to remove the sac. Moreover, pressure of the ovum on the ureter led to pyonephrosis and disorganization of the right kidney which necessitated its removal. A part of the ureter is seen in the specimen adherent to the sac. When examining specimens of this kind it is important to differentiate between true intraligamentary pregnancies and intraperitoneal gestations covered by adventitious capsules.

The following criteria should be looked for: (*a*) The relations of the ovum to the broad ligament and uterus should be those of a broad ligament cyst; the folds of the broad ligament should be completely flattened. (*b*) The pelvic peritoneum and the peritoneum of the anterior abdominal wall should be found detached from the cellular tissue and covering the tumour. (*c*) The ovary should be flattened on the surface of the sac and the uterus should be closely applied to it. (*d*) The round ligament should be intimately related to the surface of the tumour. (*e*) Muscular tissue should be found in the sac wall.

The relative frequency of termination in ectopic pregnancy in this series differs considerably from that of different series published.

In a series published by Frank[24] the proportion between tubal rupture and expulsion of ovum into the peritoneal cavity was equal for the two terminations.

Compared with Polak's[25] series of 307 cases our results were as follows:—

	Our series (per cent)	Polak's series (per cent)
1. Unruptured	10	12
2. Intra-tubal rupture with partial or complete expulsion of ovum ...	27	64
3. Actual rupture into the peritoneum	58	6
4. Rupture into the broad ligament ...	5	14
5. Undetermined	0	4

This considerable variation cannot be accounted for by the simple explanation often quoted that the class of patient is different in the different series.

Development to Term Without Rupture of the Fallopian Tube.

The ability of the tube to accommodate the foetus to term without rupture is doubted by most writers. Scepticism on this point is only too natural when we consider the small calibre of the tube, and the size it should develop to if pregnancy goes to term. Out of the 16 cases of this variety collected from literature by F. Jayle and Delherm[26] in which pregnancy was claimed to have advanced beyond the fifth month, very few were accepted as proved examples. Yet I have in my museum 3 specimens which fulfil the most rigid criteria (Figs. 12, 13 and 14). The exact anatomical relations of the sacs were verified in each case. Microscopical sections of numerous portions of the sacs removed from different situations were examined by my colleague, Dr. Sourour Bey, Assistant Professor of Pathology, who found muscular fibres in all the sections examined. I have, moreover, been able to trace the relation of the lumen of the tube to the foetal sac in both poles of the specimens. In 2 out of the 3 cases the abdominal ostium was dilated to the size of a half-crown piece, a thin membrane being attached to the edges. During the operation for removal of these specimens the ovaries were found at a distance from the sacs and not incorporated in their wall. The sacs after separation of the adhesions became quite mobile and possessed a longish pedicle.

Rarer Varieties of Ectopic Gestation.

Three varieties of ectopic pregnancy are considered to be of rare occurrence, viz., the interstitial, the ovarian, and the abdominal.

Interstitial pregnancy. This is supposed to be the rarest of ectopic implantations. Records of 79 cases were collected by Moore[27] between 1893 and 1922. Many more cases have since

been reported. The first case was found by Traub[28] at an autopsy. In 1893 he discovered another interstitial pregnancy in a uterus which he removed by subtotal hysterectomy. In the same week Lawson Tait[10b] described another case which he discovered unruptured while operating on a patient supposed to be suffering from a suppurating cyst of the broad ligament.

In our series 4 cases occurred. In 3 of these rupture with severe intraperitoneal haemorrhage occurred towards the end of the second month. In the fourth case a tubal mole was found. Rupture of interstitial gestations is said to occur at a later date than is usual with the other varieties. This is attributed to the fact that a layer of dense muscular tissue intervenes between the ovum and the peritoneal cavity. Demelin and Richard[29] described a rare case in which gestation progressed unruptured till the fifth month, and Bar[29a] met with a case which remained unruptured till the seventh. The diagnosis of this variety of tubal pregnancy before rupture is apt to offer considerable difficulties. In many cases the patient's symptoms are so trifling that severe intra-peritoneal haemorrhage may occur without warning. (Fig. 1).

Ovarian pregnancy. This condition was first described by Mercerus in 1614. The possibility of its occurrence was, however, denied by most writers. During the last few years several well-authenticated cases have been published. Up to 1878 there did not exist any criteria by which such cases could be judged. In that year Spiegelberg reported what he believed to be a conclusive case, and formulated the conditions which must be fulfilled in order to justify such a diagnosis. Twenty years later Catherine Van Tussenbroeck presented at the Congress of Medicine at Amsterdam a case in which the ovum developed in the Graafian follicle. The evidence of ovarian pregnancy in this case was definitely accepted.

Meyer and Wynne[30] in 1919 were able to collect 42 cases from the literature. Rubin in the same year recorded 21. L. A. Sutton,[31] by 1924, had assembled 72, of which he accepted 47 as fully authentic.

Most cases terminate by early rupture and intraperitoneal haemorrhage. In 2 cases recorded by Munro-Kerr[32] early rupture occurred, but in the cases published by Banks and McCann[33] rupture occurred at a comparatively later date. Patients who reached term have been recorded by Grimsdale[34] and Brugnatelli.[35]

In our series there are 3 cases which fulfil Spiegelberg's

criteria, but, to my mind, only 1 of them should be accepted as primarily ovarian.

The operation on this patient was performed by Prof. Roy Dobbin. Fig. 15 is a sketch of the specimen which he made when he removed it in 1910. This valuable specimen has mysteriously disappeared from our museum. In the second case (Fig. 16) the foetal sac occupied the position of the ovary, and was connected to the uterus by the ovarian ligament, but ovarian tissue was found only in a few places. Moreover, two-thirds of the tube of the same side were left behind and, therefore, were not available for microscopical examination. In the third case neither an embryo nor chorionic villi were found. This case was more like a ruptured ovarian haematoma than an ovarian pregnancy.

Abdominal pregnancy. Primary abdominal pregnancy, though theoretically possible, is doubted by most authors. I have never met with a convincing case. In our series there are, however, 2 cases which may be considered instances of this variety. I shall, therefore, describe them with some detail.

In December 1930 I was called to see a patient who was suffering from right-sided abdominal pain. She was 27 years of age and had been married for 3 years. I had delivered her 6 months previously of a full-time child whom she was still nursing. On examination I found a lump on the right side which appeared to me to be an unruptured tubal pregnancy. My colleague, Prof. Roy Dobbin, saw the case in consultation with me 2 days later. He concurred with my diagnosis. An operation was proposed but the patient declined. A fortnight later the pain became so severe that I was again asked to see the patient. While examining her bimanually I felt the Fallopian tube collapse under my fingers. The pain immediately disappeared, and, contrary to that which I expected, urgent signs of internal haemorrhage did not occur. Ten days later severe intraperitoneal bleeding took place. I opened the abdomen and found a 2 months' ovum implanted upon the mesentery of the sigmoid flexure. The Fallopian tubes appeared to be quite normal and did not show any naked-eye changes of recent distension whatsoever. The ovaries also appeared to be quite normal. It is evident that in this case gestation was originally tubal, the ovum was expelled out of the tube and implanted itself on the mesentery. Had I not examined this patient when the ovum was inside the tube, I would have taken the case for a primary abdominal gestation. Fig. 17 is an illustration of the second case of abdominal preg-

nancy. It is a case of twin pregnancy. One of the twins had died at an early date, while the second developed till term. The placenta was attached to the uterus, broad ligament and intestines. The ovaries and Fallopian tubes appeared to be quite normal. The history of the patient was that of a straightforward pregnancy except for an attack of severe abdominal pain followed by collapse somewhere about the second month. False labour followed by death of the foetus occurred at term.

Fate of the extra-uterine foetus. When the ovum is expelled into the peritoneal cavity, whether by intraperitoneal rupture or tubal abortion in the early weeks of pregnancy and the patient survives, the ovum dies and is absorbed. On the other hand, expulsion into the peritoneal cavity may occur, as pointed out by Berkeley and Bonney, through a perforation made by the trophoblasts in the tubal wall. If no large vessels are opened up and the haemorrhage is not very severe, the detached part of the chorion may become attached to the omentum or intestines or pelvic peritoneum. Under these conditions pregnancy may (if the amnion is intact) persist up to term without giving rise to symptoms that suggest that pregnancy is in any way abnormal. If the foetus in these cases is not removed by operation, false labour will set in. A uterine decidual cast is expelled and the foetus dies. If the dead foetus is not removed by operation putrefaction or septic infection may occur. If an abscess forms it usually bursts into one of the hollow viscera, or through the abdominal wall. The abscess may continue to discharge for years, and fragments of the foetus will come away piecemeal. In some cases, however, the sac remains free from infection, and the amniotic fluid will become absorbed. The foetus will then either dry up and become mummified or else lime-salts will deposit in the skin and the deeper tissues and the foetus will be turned into a lithopaedion. Calcification of the foetus may occur in tubal as well as in abdominal pregnancies (see Figs. 19, 20A and 20B).

According to Winckel[36] half of the foetûs in ectopic pregnancy are deformed. In our series, however, the foetûs which advanced till term, whether outside the tube or inside it, showed little or no abnormality and would have certainly been saved had the patients come to us in good time. On the other hand some of the foetûs that died at an early age showed marked malformations. These were in all probability due to nutritional deficiency induced by faulty placentation. Fig. 11 represents a case of intra-ligamentous pregnancy which proceeded to term and in which the mother herself was to blame for losing her only chance for having a living

baby. Fig. 18 is an illustration of a case in which the foetus was skeletoned, the sac suppurated, and the abscess burst through the abdominal wall. The patient was a Sudanese woman 34 years of age and had 4 children. The retained suppurating foetus did not cause any trouble, and, according to her statement, pregnancy differed in no way from the natural.

When I examined this patient I found a lump adherent to the anterior abdominal wall. A sinus at the umbilicus connected with this lump was discharging pus. An X-ray examination revealed the presence of shadows of foetal bones. At the operation I dilated the sinus with laminaria tents sufficiently to admit a finger, and removed the bones which are seen in the figure. They belonged to a twin pregnancy. The soft parts had been totally absorbed. The bones alone remained.

In the literature the incidence of occurrence of lithopaedions is considered to be about 3 per cent. In the Mayo clinic series[37] it was 2 per cent. In our series it was about 3 per cent (Figs. 19 20). In 1 of our cases the calcified products of conception had been carried for 4 years without producing any symptoms. In another case it was carried for 15 years during which space the patient had 4 living babies. It was only during the birth of the fourth baby that the lithopaedion caused symptoms sufficient to force the patient to come for treatment. In the literature there are many examples of extreme tolerance in women who carried calcified foetûs for several decades without the slightest discomfort. At a meeting of the Royal Society of Medicine, held in London on April 3rd, 1919, Herbert Williamson showed a specimen from the museum of St. Bartholomew's Hospital of a lithopaedion which remained in the mother's abdomen for 50 years until her death at the age of 80. This same specimen had been exhibited at the Obstetrical Society 105 years previously by Brown Cheston and Sir William Lawrence. According to D'Aunoy and King[38] the first mention of a lithopaedion occurs in Bauhin's *Gynaeciorum*.[39] This is the classical lithopaedion of Sens reported by Cordaeus in the sixteenth century. Brainbridge,[40] on the other hand, regards as first on record the case described by Israel Spach in an extensive gynaecological work published in 1597, where a lithopaedion is drawn *in situ* with the mother's belly laid open. Spach attributed the presence of a stone foetus in a human belly to the reversal of things to the conditions which existed after the Flood. He tells us that the world was then repopulated by the two survivors, Deucalion and Pyrrha, who walked over the earth and cast

stones behind them. On striking the ground these stones became people. An epigram dedicated to the calcified foetus reads as follows:—

> Deucalion cast stones behind him and thus fashioned our tender race from hard marble. How comes it that nowadays, by reversal of things, the tender body of a little babe has limbs nearer akin to stone?

(I wonder if Bauhim's and Spach's lithopaedion may not be one and the same?)

Unusual complications. Before entering on the clinical part of the subject I wish to refer to some rare occurrences in ectopic gestations.

Hydatidiform moles. A number of instances of hydatidiform degeneration of an ectopic mole is recorded. In 1919 A. W. Meyer[41] was able to report 48 new cases in which he discovered hydatidiform degeneration.

Chorion-epithelioma as a sequel to tubal pregnancy has been reported by Solomons and Smith.[42] Cope and Kettle[43] collected 15 cases of which 3 recovered.

Bilateral tubal pregnancy. Eighty-two cases of bilateral tubal pregnancy have been recorded, but only 32 of these are accepted as genuine by Proust and Buguet.[44] In our series it occurred once only. Parker[24] reported a case of triplets in a patient he operated upon for intra-peritoneal rupture of a pregnant tube. At the operation he discovered an unruptured tubal pregnancy on the opposite side. Four days later the patient aborted a 6 weeks' intra-uterine pregnancy.

Combined intra- and extra-uterine pregnancies. The first case of combined pregnancy seems to have been recorded by Duverney in 1708. Weibel, in 1905, collected 119 cases. Novak,[45] of Baltimore, published a report of 276 cases including 2 of his own.

In most of these cases early rupture of the pregnant tube occurred. In 9 cases both children have been delivered alive. In some others the intra-uterine foetus died and the extra-uterine foetus was delivered alive.

Unusual sites. Tubal prenancy in the stump of a resected Fallopian tube has been described by Vineberg[46] and others. Auvray[47] gives the literature of 11 such cases.

Four cases of tubal pregnancy in the sac of an inguinal hernia have been collected by Birmann.[48]

Signs and symptoms. In our series the four cardinal symptoms of ectopic pregnancy, viz. amenorrhoea, repeated attacks of pelvic pain, irregular uterine haemorrhage, and the passage of a decidual cast were seldom present together. Many of the symptoms were absent. Pain was present in 65 per cent, irregular haemorrhage in 70 per cent, but the passage of a decidual cast was obtained in only 25 per cent of the cases. In many of our cases these uterine casts were expelled 2 or 3 days after removal of the pregnant tube. Amenorrhoea, the valuable symptom which may put the patient on her guard, was present in 35 per cent of our cases only. Many cases were met with in which severe internal haemorrhage occurred in patients who had not missed a period and were not suspicious of being pregnant.

The histories obtained from patients in our series in whom pregnancy advanced to term, differed little from those of intra-uterine gestations except that pain was more frequently complained of. Pressure symptoms were present in a few cases in which the sac had descended low in the pelvis. After death of the foetus signs of peritonitis and septic absorption supervened in 4 cases. In cases in which a haematocele formed, bearing-down pains, between the front and back passages, with feelings of pressure on the bowels and tenesmus were often complained of.

Differential diagnosis. The diagnosis of tubal pregnancy before rupture is always difficult and mistakes are frequently made even by the most experienced surgeons.

Before rupture. An unruptured pregnant tube is easily confused with an intra-uterine pregnancy complicated by a unilateral pelvic swelling. (Figs. 21 and 22). In both conditions the uterus enlarges and the signs and symptoms of pregnancy are present, but the enlargement of the uterus in ectopic pregnancy is peculiar. The uterus is less globular in form, and lacks the soft cystic, ill-defined feel of the ordinary intra-uterine pregnancy. Some cases are indeed very puzzling. In a case of this kind I thought it justifiable, before opening the abdomen, to make a lipiodol skiagram. The shadow obtained made it clear that an intra-uterine pregnancy existed. Fortunately an untoward accident did not occur and the pregnancy proceeded undisturbed.

The presence of one of the rarer combinations should not be lost sight of. About 12 years ago I was asked to see a case in consultation with the late Mr. Madden. The patient had miscarried a 4-months' baby 6 days previously. The ovum was expelled complete. On the third day after her miscarriage the

patient had a sudden attack of severe pelvic pain followed by symptoms of collapse. We diagnosed ruptured ectopic pregnancy, opened the abdomen and removed a ruptured tube with a 4-months' foetus attached.

Treatment.

In 1873 Barnes[49] summed up the treatment of ectopic gestation as follows:—

> In the case of tubal gestation, there being no available outlet, we are precluded from the induction of labour. But the embryo may be killed and thus development in the sac cut short. . . .
>
> Dr. Bacchetti described a case in which two needles were passed into the tubal sac, and then a current of electricity was passed through by means of Bunsen's pile. Two shocks were administered. The growth of the tumour was arrested and the patient did well.
>
> Many attempts in ancient and modern times have been made by starvation and drugs to accomplish this object. . . . Syphilis has more power than almost any poison we are acquainted with over the foetus, always either killing it, or impeding its development. Might it not be justifiable, in such a case as we are discussing, to practise syphilization? I do not dwell upon this repulsive method, because I believe simple puncture of the sac is the right course to adopt.
>
> The question has often been discussed, whether it is not advisable to check bleeding by tying the Fallopian tube on the proximal side of the sac and cutting away the tube. I can hardly imagine that this idea will ever be successfully carried out. Removal of the blood must add to the shock, and to discover the source of bleeding and to remove the blood is by no means easy. Moreover, the pain caused by the ligature will probably be so intense as by itself to exhaust the vital power.

Four years later the treatment of ectopic pregnancy was revolutionized by Lawson Tait,[10] who deliberately opened the abdomen and removed the pregnant tube. The following most instructive passages taken from his book *Diseases of Women and Abdominal Surgery*, published in 1889, are worthy of our consideration:

> In the summer of 1881 I was asked by Mr. Hallwright to see with him in consultation a patient who had arrived by train from London. . . . The illness had been diagnosed by Mr. Hallwright as probably haemorrhage into the peritoneal cavity from a ruptured tubal pregnancy. . . . I agreed with him as to the nature of the lesion. This gentleman made the bold suggestion that I should open the abdomen and remove the ruptured tube. The suggestion staggered me and I am ashamed to say I did not receive it favourably. . . . I declined to act upon Mr. Hallwright's request and a further haemorrhage killed the patient.
>
> A post-mortem examination was made . . . and I found that if I had

> tied the broad ligament and removed the ruptured tube . . . the patient's life would have been saved. A most striking contrast to this terrible incident will be found in the following case when, thanks to the ability and firmness of Dr. Dolan, of Halifax, I was able to save a valuable life.

Tait then gives us a description of the first case in which he successfully tied and removed the pregnant tube and concludes by saying:—

> This I have done now in 39 cases with one death, and I think I may fairly say that I have really achieved a surgical triumph. My example has been widely followed and the success is almost uniform.

His wise comment on the 1 fatal case in his wonderful series is worth noting:

> I wasted much time in trying to stop this haemorrhage. . . . I had blundered. The true method of operating in such cases was to separate adhesions rapidly, regardless of the bleeding, and make at once for the source of haemorrhage, the broad ligament, tie it at its base and then remove the ovum, debris and clots at leisure.

The treatment of ectopic pregnancy nowadays differs very little from what Lawson Tait taught us 55 years ago, except for modifications made to meet the different phases met with.

1. *Unruptured tubal pregnancy.* In the rare cases in which a positive diagnosis of ectopic gestation is made before rupture of the pregnant tube, the gravid tube should be removed without delay. Within recent years, however, the question of advisability of adopting such a radical measure in every case was raised. Blair-Bell and Whitehouse[50] proposed that in certain cases at least a more conservative operation may be done. Salpingotomy with enucleation was suggested as an alternative to salpingectomy.

The main objection to this conservative plan is that repetition of pregnancy in the same tube has been frequently known to occur. In 1901 Pestalozza[51] collected 111 cases in which tubal pregnancy occurred in the same patient a second time. R. R. Smith[52] states that among 1,608 tubal pregnancies operated upon by members of the American Gynecological Society 58, or 3.6 per cent, had subsequent extra-uterine pregnancies. In 4 of my cases tubal pregnancy occurred a second time in the same patient. In one of these gestation occurred in a portion of the tube which I had deliberately conserved. Yet in spite of this I am still of opinion that in certain cases a conservative operation is quite justifiable, as for instance in the case of a childless young woman anxious to have an offspring. Many a time I have been earnestly

requested by a patient upon whom I was going to operate for ectopic gestation to use every endeavour that the operation should not make a future pregnancy impossible. If the patient's condition allows, I always try to perform a conservative operation on the pregnant tube and a plastic operation on the tube of the other side as well if it were blocked. In my experience 4 childless patients on whom I performed plastic operations on the blocked tubes intra-uterine pregnancy subsequently occurred. Even in interstitial pregnancies (Fig. 22A) a conservative technique can sometimes be followed. The pregnant cornu may be excised by a wedge-shaped incision. The remaining portion of the tube, if healthy, may also with advantage be implanted in the uterine cavity. Prof. Roy Dobbin has successfully performed this operation on two occasions (Fig. 23). Such conservative procedures are, however, only possible when we are dealing with very early cases. In advanced cases such treatment would be fraught with considerable difficulty and is not free of danger. Hysterectomy is the only safe procedure.

2. *Diffuse haemorrhage.* If the haemorrhage is diffuse the patient's condition is in most cases so bad that time cannot be lost on plastic operations. The pregnant tube should be quickly removed. Some difference of opinion still exists on the advisability of immediate operation in cases in which signs of marked shock are present. A few writers advise waiting until the patient's condition improves. The overwhelming majority of authorities, however, rightly insist upon immediate operation. In many of our cases the patients were in a marked state of collapse, yet they were all saved by immediate interference. The shock was not increased in any of the cases by operation. In fact many of the patients showed signs of improvement when the abdomen was cleared of the effused blood. Placing the patient in the Trendelenburg position and infusing with salt solution, hypertonic glucose or gum acacia, is undoubtedly very wise but should only be commenced during the operation and not before it. Blood transfusion, when necessary, if an available donor is found, may be administered, as soon as the grouping is settled.

3. *Encysted haemorrhage.* Small encysted haematoceles may be readily absorbed under expectant treatment. In the large majority of cases the ovum is dead. If the haematoma becomes larger instead of diminishing in size interference is necessary. The ovum is in all probability still alive, and fresh attacks of haemorrhage are occurring. A Zondek-Aschheim test may in these cases be of help. A positive result is an indication for laparotomy

even if the haematoma be small. A negative result in a haematoma which does not show any signs of growing is an indication for expectant treatment.

Large haematoceles should always be dealt with abdominally. The sooner this is done the better. In old standing haematoceles the organized blood-clots adhere to the adjacent tissue very densely and may cause damage to the intestine when separating them at operation.

In cases in which infection of the haematocele is suspected vaginal drainage should be adopted.

4. *Advanced tubal pregnancy*. The question of dealing with advanced ectopic pregnancy was thoroughly discussed at a meeting of the Royal Society of Medicine held in April 1919. Ley, Andrews, Giles, Hedley, Fairbairn and Eden took part in the discussions. The consensus of opinion was in favour of early operation irrespective of whether the foetus was alive or dead. Fairbairn pointed out that, in his experience, the most severe and ultimately fatal haemorrhage during removal of the placenta occurred in those cases in which the operation was performed after death of the foetus; whereas in a case in which a living foetus was delivered by laparotomy before term there was not, practically, any haemorrhage and the mother and child recovered without complications. He rightly pointed out that it was the situation of the placenta far more than the activity of the circulation which determined the amount of haemorrhage. Eden stated that he had operated on 2 cases in neither of which had he had any difficulty with haemorrhage. He agreed that the operation should be done at once.

Immediate operation has in recent years become the accepted practice. In exceptional cases, however, when the child has nearly attained the period of viability, the patient is childless and anxious to have a living baby, the operation may be delayed for a few weeks. The patient should in these cases be placed under observation in a hospital. If signs of rupture of the sac occur at any time the operation can then be done without delay. In the one case in our series in which the child was alive, the patient was kept in hospital under observation for 4 months. Prof. Shafeek Bey operated about the end of the eighth month. The sac had burst the night before and the foetus was lying free in the peritoneal cavity. The placenta was attached to the floor of the ruptured tube, to the uterus, the broad ligaments, and intestines. There was not, however, any difficulty in peeling off the placenta. The bleeding which accompanied separation was

unimportant. The patient did very well, but, unfortunately, the baby succumbed to double pneumonia a fortnight later.

In the 3 cases in our series in which pregnancy proceeded to term inside the tube, the operation did not offer any difficulty. Convalescence was remarkably uneventful. In contrast to this, great difficulties were met with in dealing with the placenta in the cases of secondary abdominal pregnancy in which the foetus was dead. In 1 of these patients Shafeek Bey removed the foetus, cut the cord short, left the placenta undisturbed, and closed the abdomen without drainage. Convalescence was uneventful, but the patient subsequently developed an incisional hernia. A few months later an operation was performed for the repair of the hernia. The abdominal cavity was searched for the placenta but it could not be found.

The second case in which the placenta was left behind (Fig. 24) presents several points of interest. The patient was a 9-para, 30 years of age. The last menstrual period occurred 10 months before she came to hospital. At the fifth month severe abdominal pain occurred at the right side and lasted for 2 days. Dull, aching pain persisted for 20 days more. There was no vaginal bleeding at any time during her pregnancy. At term symptoms of labour began and persisted for 2 days. Foetal movements stopped and pains died away. A month later the patient came to the hospital for consultation. On examination the cervix admitted one finger. The head was felt through the anterior fornix. Abdominally, the foetal parts were indistinct. Foetal heart-sounds were not heard.

The patient was operated upon 2 weeks after admission. The sac was reached by a sub-umbilical incision. The foetus was found macerated and the contents of the sac were stinking. The fluid contents were removed and the child delivered. It was fully developed and weighed 8 pounds. An effort was then made to remove the placenta, but it had to be given up on account of the haemorrhage which followed separation. The sac was marsupialized. The incision in the abdominal wall was only partly closed. The cavity of the sac was packed with gauze which was changed daily. Three weeks later the patient, who was supposed to be progressing favourably, suddenly collapsed and died. At the autopsy peritoneal adhesions and ascites were found. The liver was the seat of fatty degeneration. The spleen was oedematous and congested. The heart was fatty and the cavities dilated.

Another case of advanced pregnancy in our series presents points of interest and deserves more than a passing mention. It

is the case of intraligamentous full-time pregnancy, which is mentioned before. The first time I saw this patient was in January 1919. She consulted me on account of sterility. She was a peasant woman 30 years of age and had been married for 10 years but had never conceived. I dilated and curetted her uterus. Two months later she missed a period and had all the subjective signs of pregnancy. I saw her then and found an unruptured right tubal pregnancy. The patient was so disappointed when I told her this that she refused to be operated on. Two months later I saw her again and found that the tube had ruptured into the broad ligament. The risks of waiting were explained to the patient, but she thought it was worth her while to run the risk of waiting in the hope of having a living baby. She, however, did not come back till 18 months after death of the foetus. Peritonitis had then occurred and the sac was infected and bound to the adjacent tissues with dense adhesions. The kidney was converted into a bag of pus. At the operation I was forced to remove, besides the sac and its contents, the uterus and the loop of densely adherent gut. The disorganized kidney and ureter were removed at the same time.

During convalescence the patient became mentally deranged for several days and tore the wound open; despite this recovery was complete.

Pregnancy in a Rudimentary Horn of a Bicornute Uterus.

This accident occurred in 5 of our cases (Fig. 25). The muscular band connecting the rudimentary horn to the cervix was atretic in 4 cases out of the 5. In 2 cases the corpus luteum was found in the ovary of the same side. The occurrence of pregnancy in such patients can only be explained by migration of the spermatozoon from the other side. In 3 cases the operation was performed at the fifth month of pregnancy, before rupture occurred. In the fourth case (Fig. 26) the patient was admitted to hospital with severe crampy abdominal pain. A decidual cast was passed the day before admission. The passage of a decidual cast raised the suspicion of tubal pregnancy, but on careful examination of the patient the broadness of the base of attachment of the mass of the uterus, the low level of its insertion and the comparative mobility of the fundus of the uterus, gave the clue to the correct diagnosis.

When the abdomen was opened the pregnant horn was found to be in a condition of incomplete rupture. The peritoneal coat alone was intact.

The fifth case (see Fig. 27) was that of a uterus bicornis with persistence of the urogenital sinus.[53] This variety of maldevelopment, or rather arrest of development, must be exceedingly rare. I have not found any mention of it in the textbooks or the literature available to me.

The development of the urogenital organs in this case was similar to that of a foetus of 10 to 12 weeks (see Figs. 28 and 29) and closely resembled the genito-urinary organs of higher mammals (*carnivora*) in which the medial walls of the Müllerian ducts are present, the uterus consists of 2 chambers separated by a septum and the vagina and urethra are represented by a urogenital sinus.

On admission to hospital the general condition of this patient was extremely bad. The height of the fundus was three fingers above the umbilicus. On examination, the vulval outlet led to a canal which could admit two fingers. At the vault of this canal two openings were seen, one of which led to the bladder, and the other to the uterus. It was evident that delivery *per vaginam* was out of the question. The abdomen was therefore opened, the uterus incised medially, and the foetus and placenta delivered. On the left side of the uterus a collection of pus was found. When this was broken through it was found to lead to a rent at the level of the lower uterine segment, which was shut off from the peritoneal cavity by recent adhesions.

The presence of this rent explains the history given by the patient of having had severe labour pains two weeks before admission. These pains lasted for 24 hours and then died out. It must have been at that time that rupture of the uterus took place.

Mortality. The mortality in different series of operations for ectopic pregnancy varies from 2 to 7 per cent; for our series it was a little under 2 per cent. We lost 2 cases. One of these was the case of advanced pregnancy in which the placenta was marsupialized, and the second was the case of pregnancy in a rudimentary horn in which the urogenital sinus persisted.

In conclusion I desire to express my sincerest thanks to my colleagues, Professor Roy Dobbin for allowing me access to his valuable library and to him and Professor Shafeek Bey for their courtesy in permitting me to include patients treated in their wards, and to my colleagues Dr. Sourour Bey and Professor Moustapha Bey Omar for the patience and thoroughness they showed in making the histological examination of specimens and the preparation of lantern slides and microphotographs. I am

also indebted to my assistants, Drs. Ismail, Magdi, Rafla, Sobhy, Roushdy, and Mazhar, and to Drs. Kawkab Nassif and Kamal, for their valuable assistance.

My thanks are especially due to Dr. Shoukry for his carefully prepared statistics, and to Dr. Boulgakow, the able curator of the museum, and Dr. F. Abadir, his assistant, for their valuable preparations and for the zeal and enthusiasm they showed in many directions, and to Mr. Strekalowsky for his beautiful drawings.

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PLATES

Illustrating Figs. 1—29

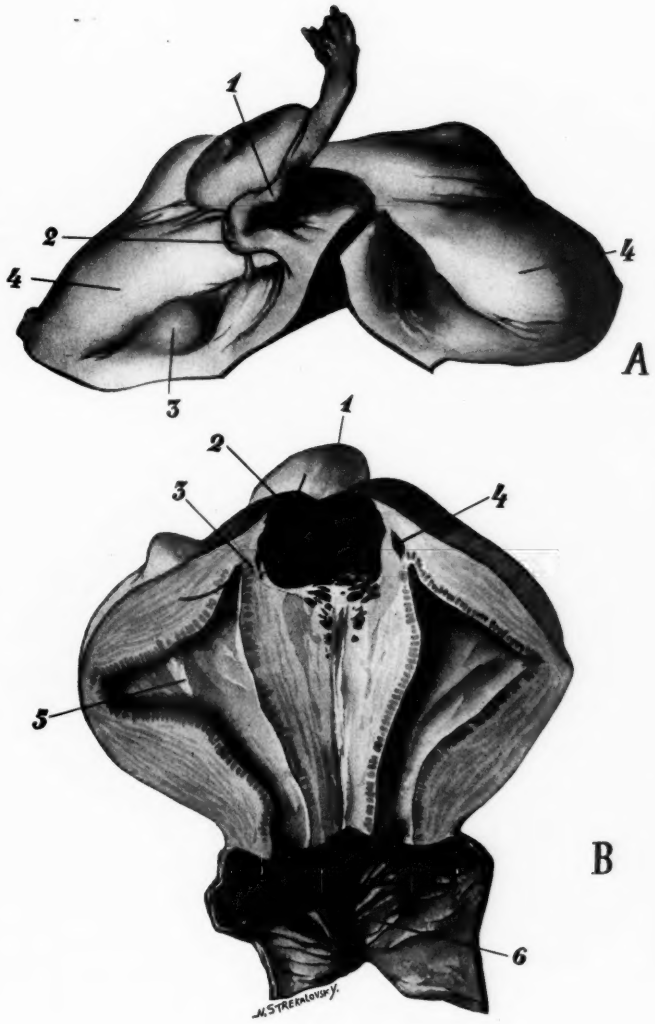

FIG. 1.

INTERSTITIAL ECTOPIC GESTATION.

(Specimen kindly presented by Dr. Emara, Medico-legal Department).

The specimen was removed from the body of a Greek woman who had a sudden attack of collapse while taking a warm bath on 10th January, 1937. A large stove had been placed in the bathroom. The patient's symptoms were wrongly attributed to carbon-monoxide poisoning and treated as such. Two hours later she died.

Post-mortem examination revealed the presence of interstitial gestation with intra-peritoneal inundation.

A. (1) Site of the first kink in the tube; (2) Site of the second kink; (3) Small myoma; (4) Body of uterus. *B*. (1) Tube; (2) Blood-clot in the interstitial portion of tube; (3) Bristle passed from the uterine cavity into the interstitial portion of the tube; (5) Uterine cavity; (6) Vagina.

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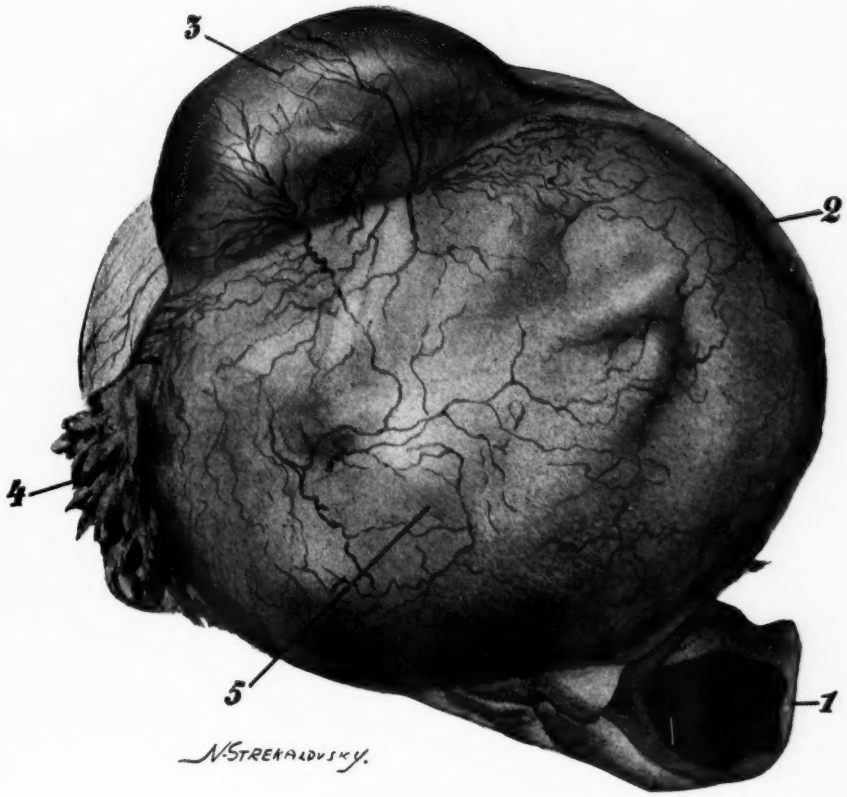

FIG. 2.

ECTOPIC GESTATION COMPLICATED BY A LARGE PAROVARIAN CYST.

(1) Ovary with corpus luteum; (2) Tube; (3) Seat of tubal gestation; (4) Fimbriated end of tube; (5) Parovarian cyst.

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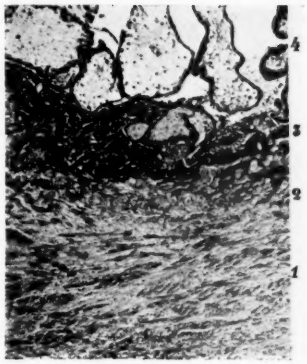

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 3. INTERSTITIAL PREGNANCY (*Sorour Bey*). Section showing: (1) Muscular coat of uterus; (2) Layers of decidual cells; (3) Zone of haemorrhage and a coagulum; (4) Chorionic villi. (High-power.)

FIG. 4. TUBAL PREGNANCY (*Sorour Bey*). Section in Fallopian tube. (1) Wall of tube; (2) Chorionic villi; (3) Haemorrhage.

FIG. 5. INTERSTITIAL PREGNANCY (*Sorour Bey*). Section showing chorionic villi in haemorrhage fields. (1) Chorionic villi; (2) Haemorrhage.

FIG. 6. INTERSTITIAL PREGNANCY (*Sorour Bey*). Section in uterine muscle wall far removed from the seat of gestation showing a vein containing a mass of trophoblastic cells mixed with red-blood corpuscles. The mass did not appear to be adherent to the vessel wall. (1) Muscle wall; (2) Wall of vein; (3) Mass of cells inside vein. The muscle and maternal veins are invaded for a long distance. A mass of syncitial cells is seen in a blood-vessel far removed from the chorion. In normal intra-uterine pregnancy invasion of the muscle wall never occurs, but syncitial cells can occasionally be seen in veins far removed from the placental site. (High-power.)

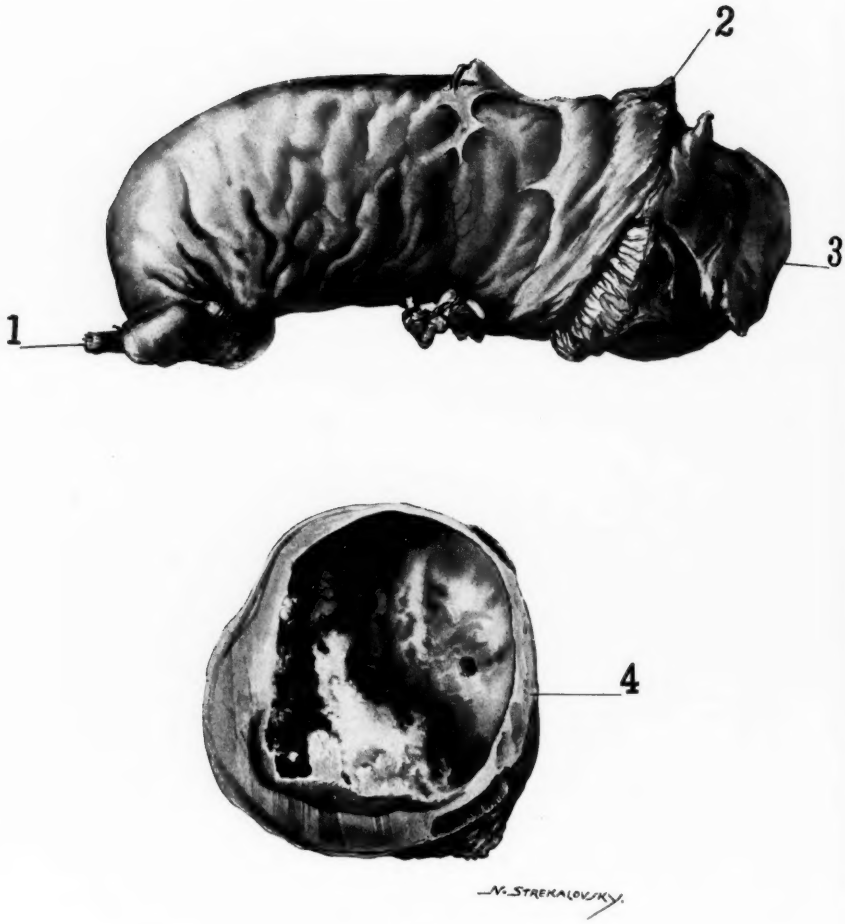

FIG. 7.

TUBAL GESTATION. INTRA-TUBAL RUPTURE, MOLE FORMATION.

The mole is seen in process of extrusion through the dilated abdominal ostium. (1) Uterine end of the tube; (2) Abdominal ostium of tube; (3) Mole; (4) Corpus luteum in ovary of the same side.

(Specimen was kindly presented by Professor Roy Dobbin.)

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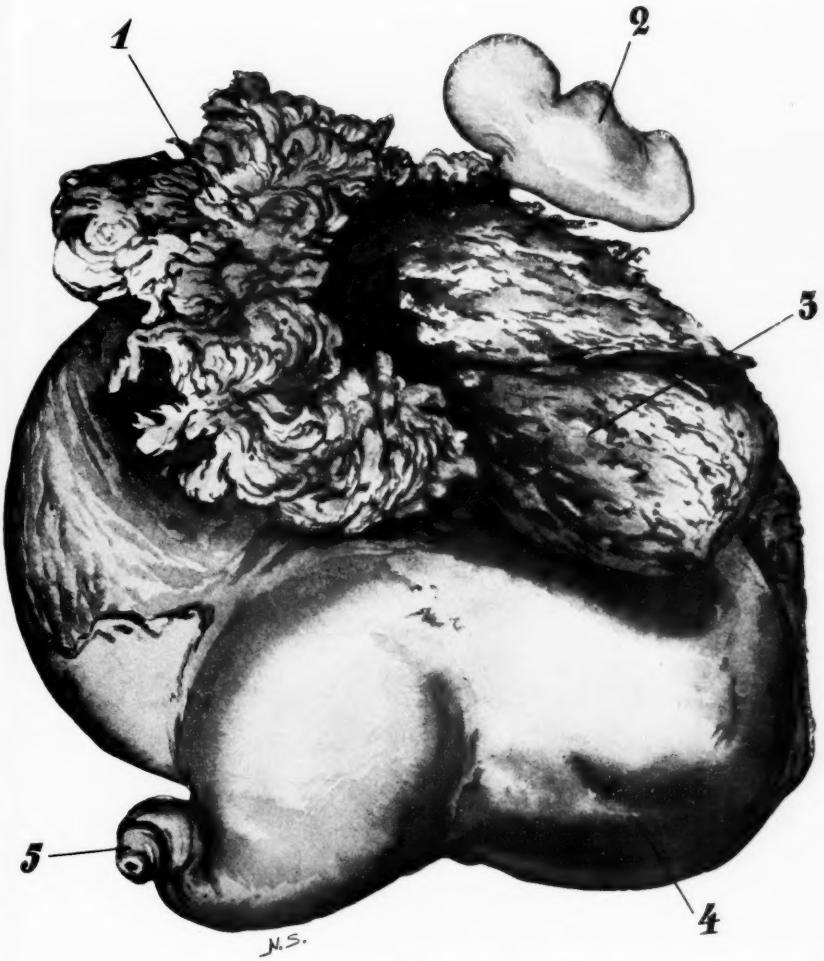

Fig. 8.

Tubal Gestation of 9 weeks' duration. Intra-tubal Rupture. The foetus and placenta are almost totally separated and extruded through the fimbriated end into the peritoneal cavity. Expulsion of the ovum was brought about by overdistension of the tube by the effused blood. (1) Fimbriated end of tube; (2) Foetus; (3) Placenta; (4) Unaffected portion of tube greatly distended with blood; (5) Uterine end of tube.

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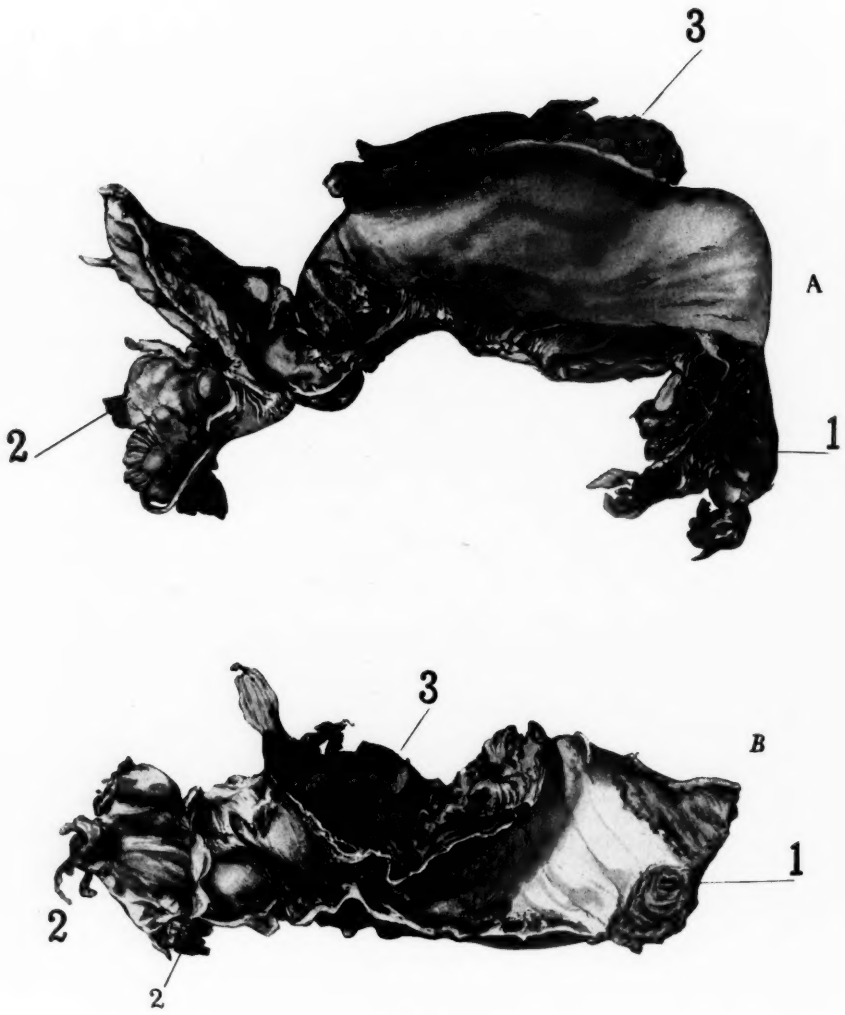

FIG. 9.

RUPTURED TUBAL GESTATION.

In (*a*) ovum was still alive (8th week). In (*b*) a mole had formed long before rupture occurred. An attack of fresh haemorrhage inside the tube caused the rupture. (1) Uterine end of the tube; (2) Abdominal ostium; (3) Site of rupture.

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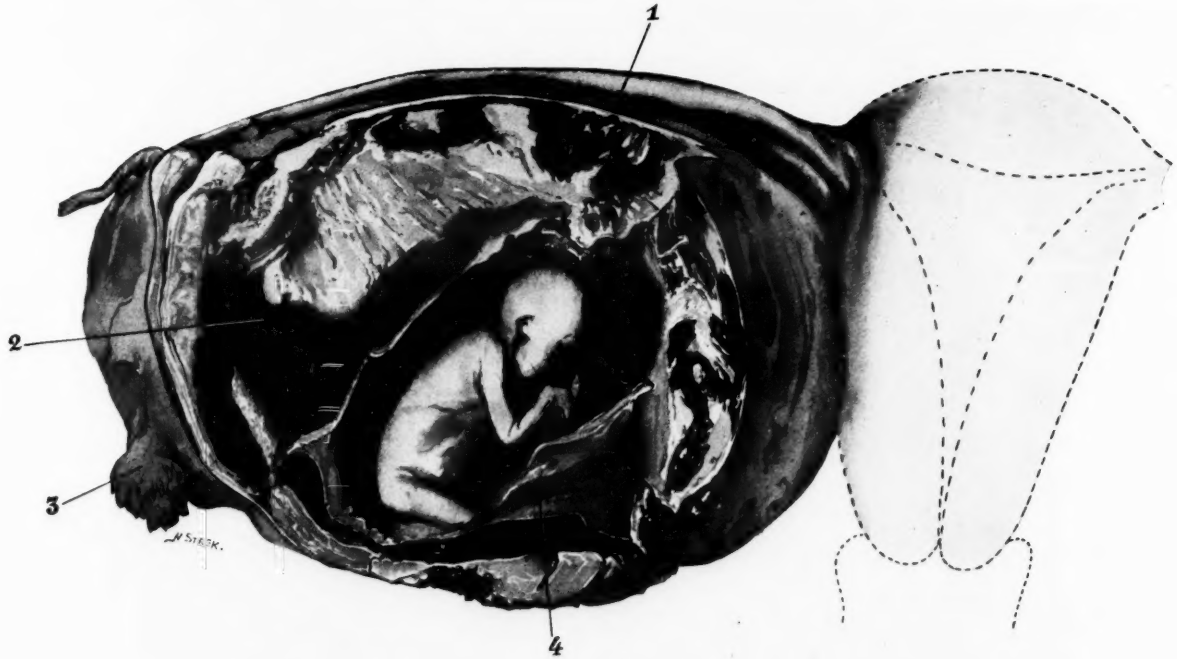

FIG. 10 A.

RIGHT INTRA-LIGAMENTOUS PREGNANCY (12 WEEKS' DURATION). The foetus and membranes are seen lying in the intra-ligamentary haematoma. (1) Tube; (2) Haematoma; (3) Abdominal ostium; (4) Foetal membranes.

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FIG. 10 B.

INTRA-LIGAMENTOUS GESTATION 12 TO 16 WEEKS' DURATION. Removed entire and opened later to expose contents. (1) Cut end of uterine end of tube; (2) Ovary; (3) Traumatic tear which occurred during removal.

F 25 B. Mahfouz's Obstet. & Gyn. Museum.

FIG. 11.

INTRA-LIGAMENTOUS PREGNANCY. FULL TERM UNRUPTURED.

(Removed entire and opened later to expose the contents.)

(1) Uterus; (2) Ureter; (3) A piece of resected gut; (4) Tube; (5) An indicator passing from the uterine cavity along the tube.

On opening the abdomen, the vesical pouch was found at the level of the umbilicus. Both layers of broad ligament were peeled off the underlying structures. The right kidney which was the seat of obstructive pyonephrosis had to be removed. A part of the ureter is seen attached to the sac which was removed entire together with the uterus.

The patient made an uninterrupted recovery, except for two weeks raving insanity during convalescence.

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FIG. 12.

UNRUPTURED FULL TERM TUBAL PREGNANCY.

(Specimen kindly presented by Professor Shafeek Bey.)

The unruptured gravid tube was removed entire and opened later to expose the contents. (1) Appendix Vermiformis; (2) Cut uterine end of tube.

FIG. 13.

FULL TERM UNRUPTURED TUBAL GESTATION.

(Specimen was removed entire and was opened later to expose contents.)

(1) Indicator passed along uterine end of tube; (2) Ovary; (3) Dilated fimbrial extremity of tube; (4) Foetal sac bulging out of ostium.

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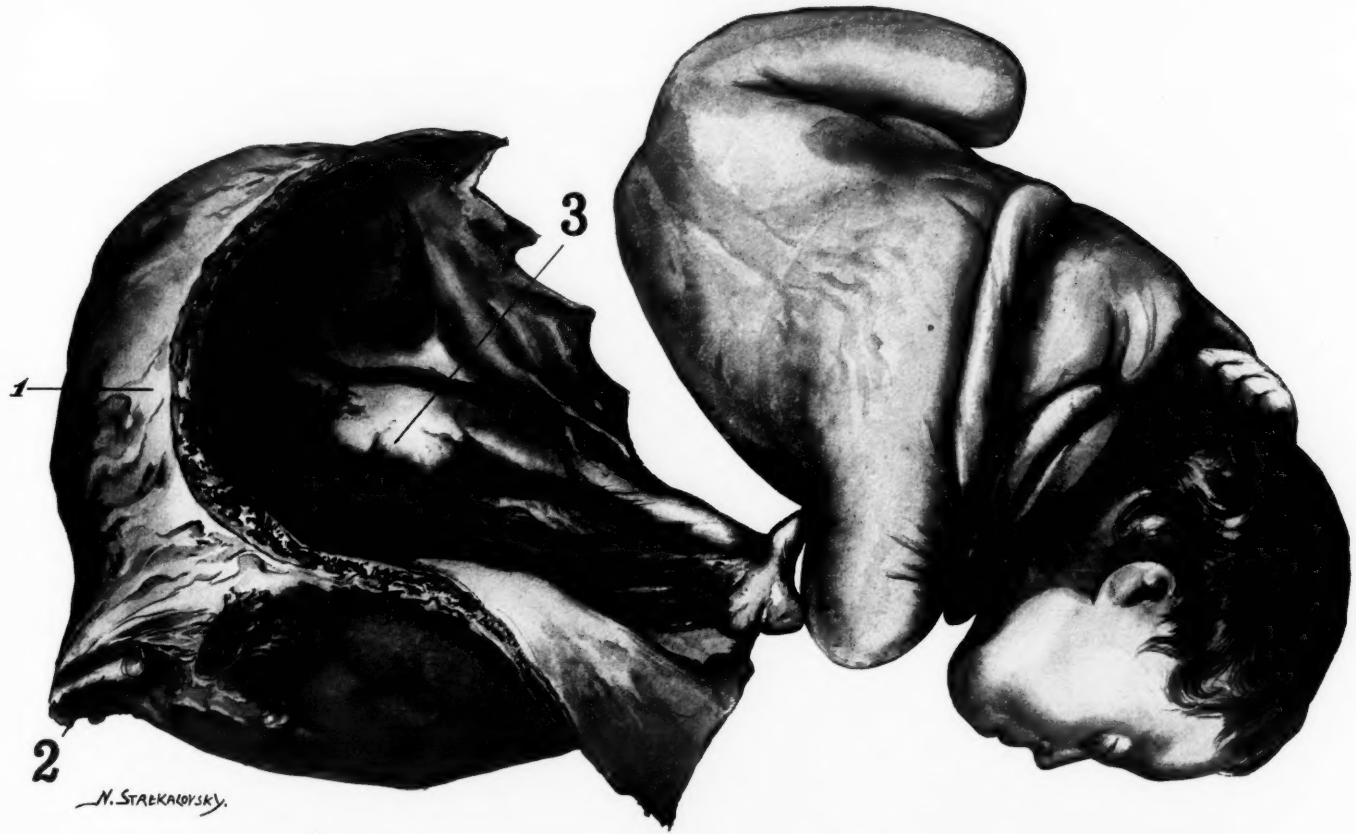

FIG. 14.

UNRUPTURED FULL TERM TUBAL PREGNANCY.

On the posterior surface of the specimen (not apparent in the figure) are seen the cut end of the ovarian ligament and the undilated isthmial portion of the tube.

(1) Distended part of the tube; (2) Undilated cut end of the tube; (3) Placenta.

Specimen was removed entire and was opened later to expose the contents.

(Specimen kindly presented by Professor Roy Dobbin.)

(Specimen kindly presented by Professor Roy Dobbin.)
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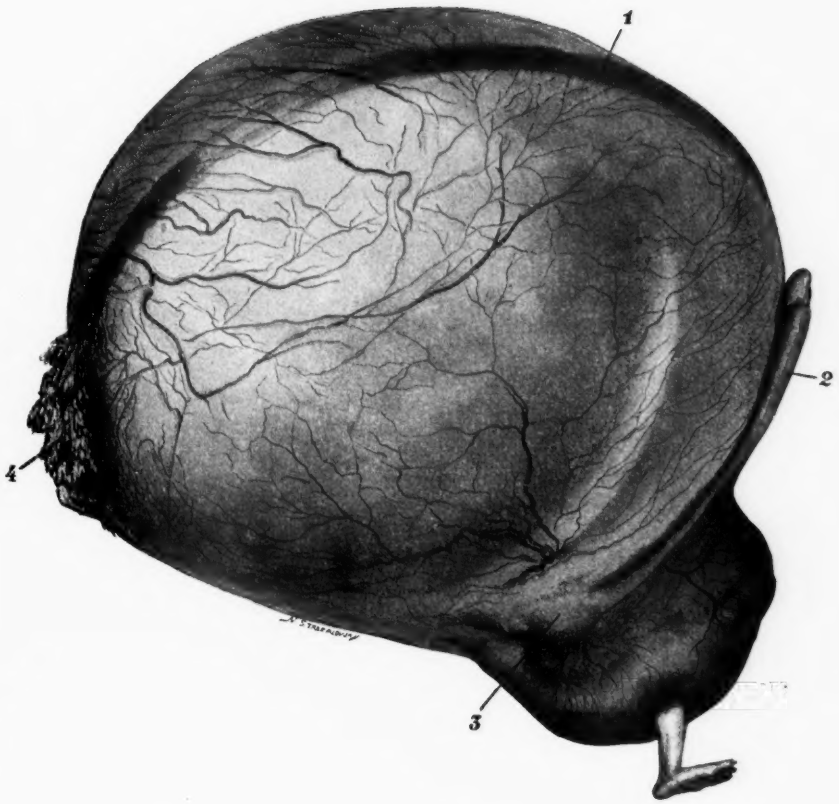

FIG. 15 A.

DRAWING OF AN UNRUPTURED FOUR MONTHS OVARIAN GESTATION COMPLICATED BY A LARGE PAROVARIAN CYST.

(Made after a sketch by Professor Roy Dobbin.)

(1) Tube; (2) Ligament of the ovary; (3) Ovary; (4) Fimbriated end of tube.

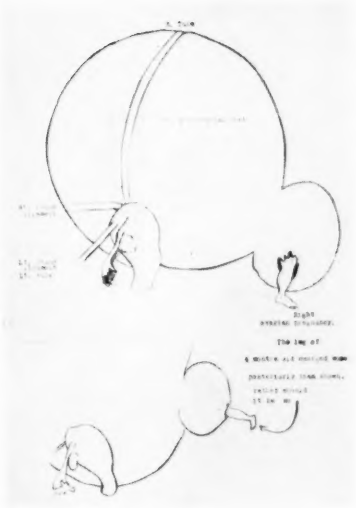

FIG. 15 B.

FOUR MONTHS' UNRUPTURED OVARIAN PREGNANCY COMPLICATED BY A LARGE PAROVARIAN CYST.

(Sketch by Professor Roy Dobbin.)

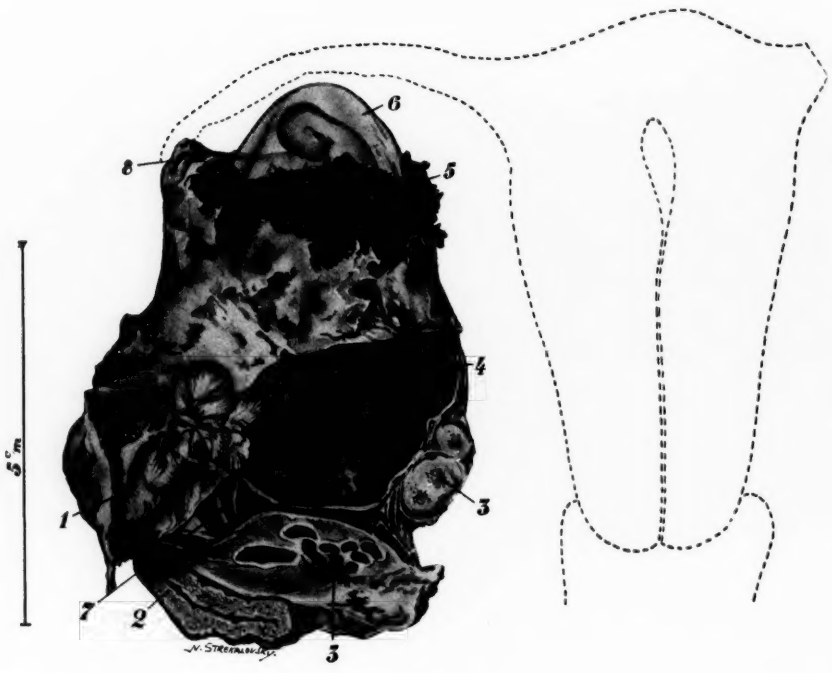

FIG. 16.

TUBO-OVARIAN PREGNANCY.

Tubo-ovarian pregnancy of 6 to 8 weeks' duration. Rupture occurred in the vicinity of the isthmic portion of the tube which was not implicated. The chorion had been torn, but the amnion remained intact, and the foetus was lying within it. The ovary was seen in section at the bottom of the specimen. It is overtopped by a haematoma which lies below the sac. The fimbriated end of the tube is seen on the left side. (1) Fimbriated end of the tube; (2) Corpus luteum; (3) Ovary; (4) Haematoma inside gestation sac; (5) Rupture at the top of the sac; (6) Foetus within amniotic sac; (7) Foetal membranes; (8) Cut uterine end of tube.

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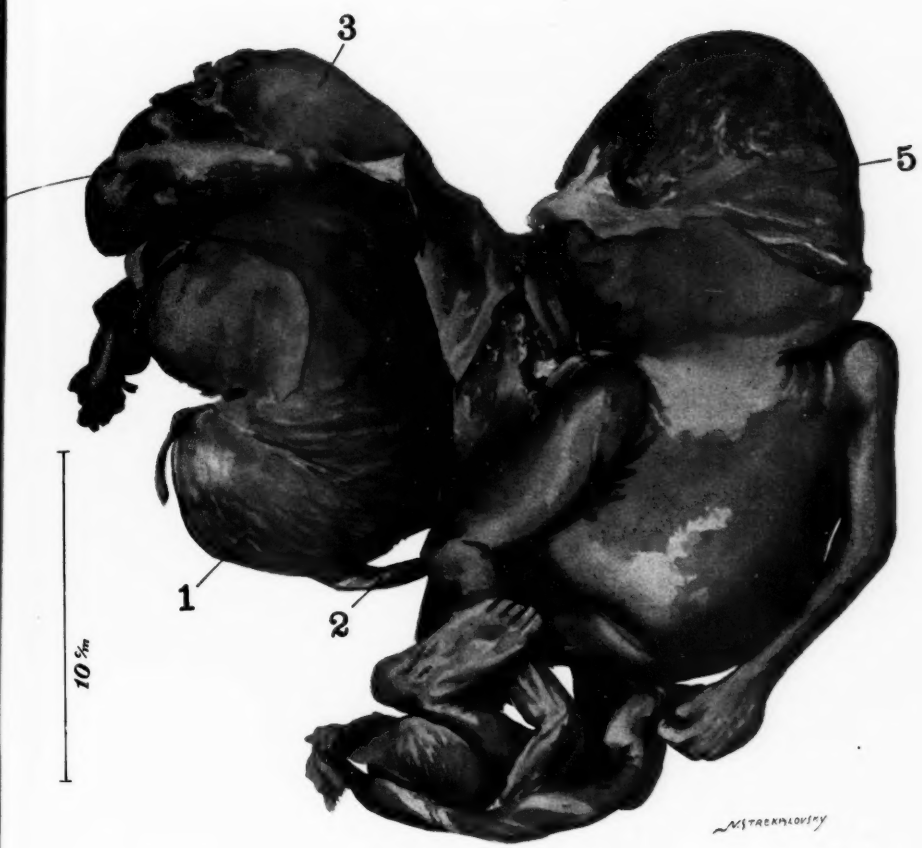

Fig. 17.

Twin Abdominal Pregnancy. (?) Primary.

(1) Placenta; (2) Umbilical cord; (3) and (4) Foetus and placenta of second ovum (verified by skiagram); (5) Adventitious adhesions.

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FIG. 18.

SKELETONIZED FOETUS (TWIN ABDOMINAL PREGNANCY).

This case is similar to the case described by Albucassis (see text).

The patient gave the following history: Six years before admission she missed seven periods. Symptoms of labour appeared, but no baby was born. The foetal movements stopped. A few months later the tumour became very painful and an abscess formed around the umbilicus. This abscess burst and kept discharging pus until patient's admission to hospital.

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FIG. 19.

TUBAL PREGNANCY OF 12 TO 14 WEEKS' DURATION. LITHOPAEDION.

The foetus has shrunk by absorption of its fluid constituents, and upon the dried tissues lime-salts have become freely deposited, converting it into a lithopaedion. The greater part of the foetus is seen extruded through the fimbriated extremity.

(Specimen was kindly presented by Professor A. Mooro.)

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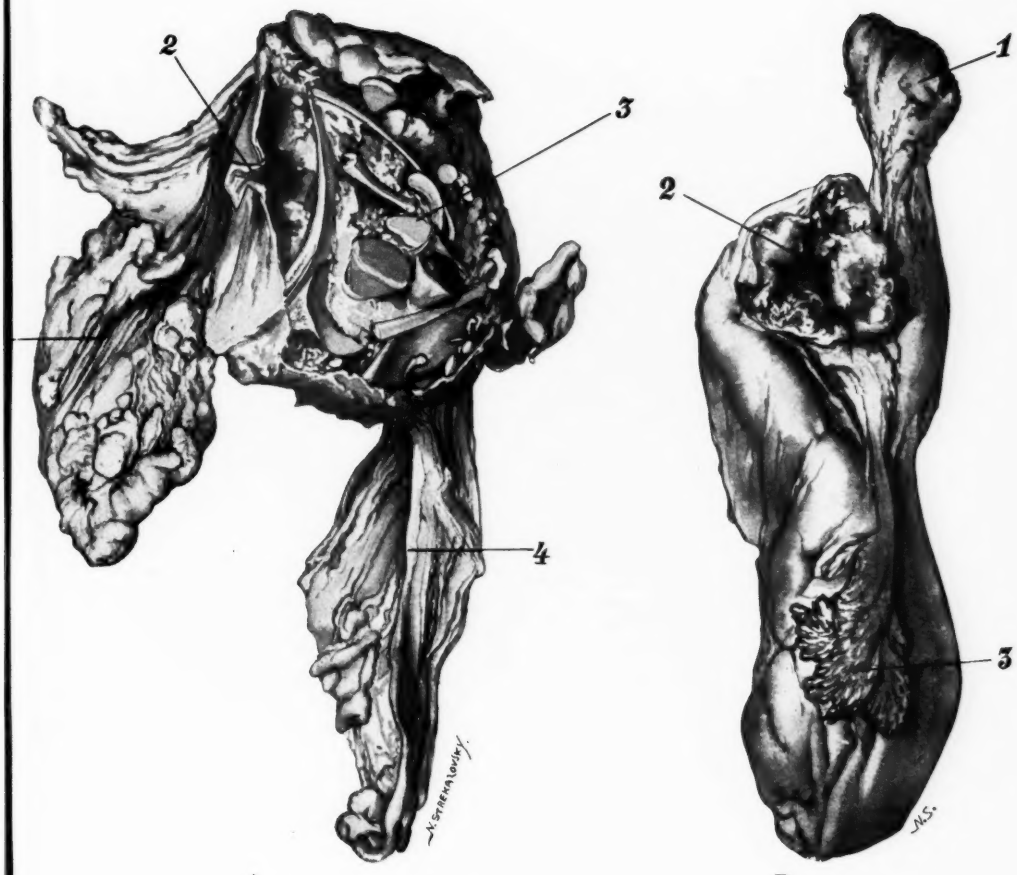

FIG. 20.

ECTOPIC PREGNANCY (LITHOPAEDION).

On opening the abdomen a lithopaedion was found almost parasitic on the omentum, a portion of which was removed with it. The body of the foetus has shrunk by absorption of its fluid contents, and upon the dried tissues lime-salts have become deposited. The patient carried her lithopaedion for 15 years.

A. (1) Omentum; (2) Foetal sac; (3) Lithopaedion; (4) Omentum which was partly adherent to cicatrised hole in tube.

B. (1) Uterine end of tube; (2) Scar at the site of rupture to which the omentum was adherent; (3) Fimbriated extremity.

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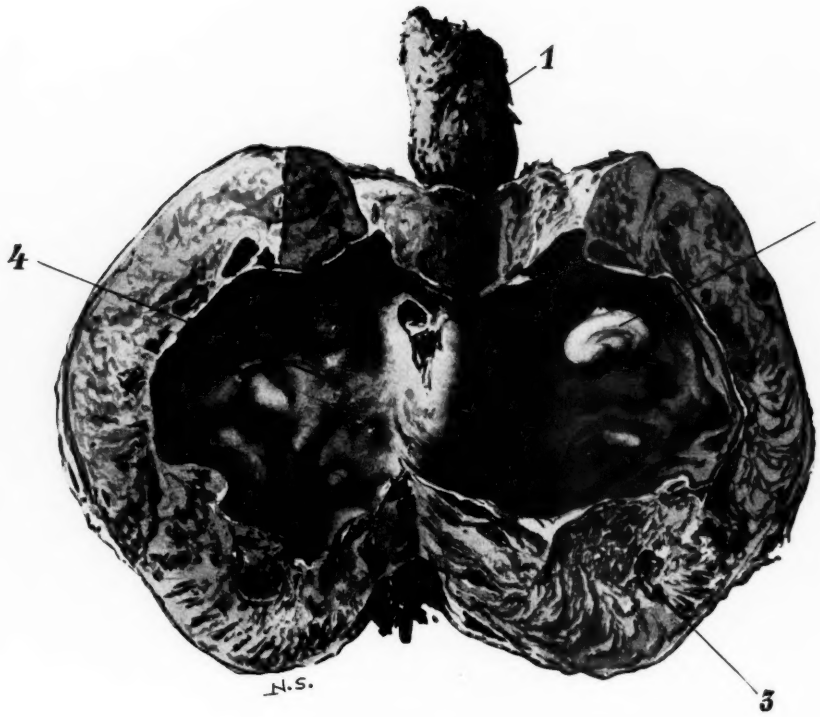

FIG. 21.

EARLY UNRUPTURED TUBAL PREGNANCY. EMBRYO ATTACHED.

(1) Uterine end of tube; (2) Embryo; (3) Chorionic villi; (4) Foetal membranes.

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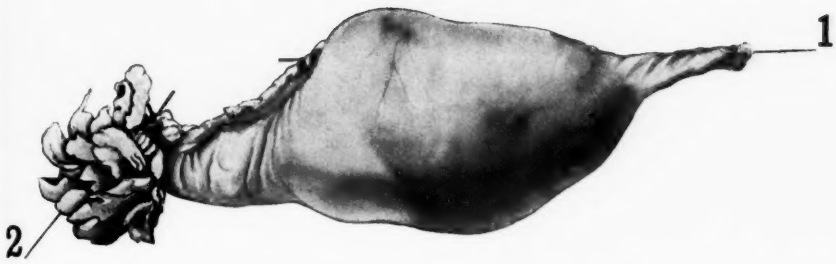

Fig. 22.
Tubal Gestation, 4 or 5 Weeks' Duration. Unruptured.
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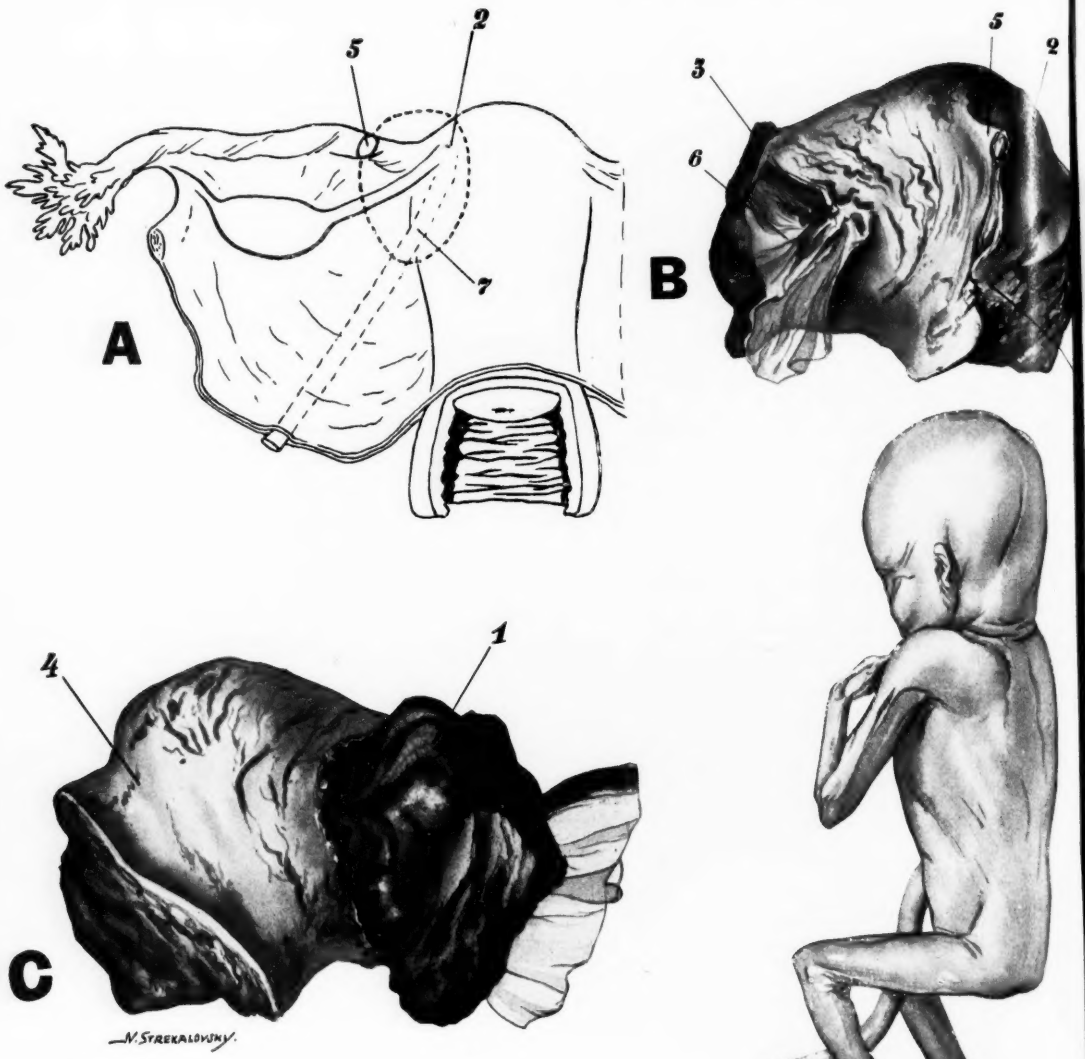

FIG. 23.

INTERSTITIAL GESTATION—RUPTURED.

A. (2) Pregnant interstitial portion of the tube; (5) Isthmic end of tube beyond the pregnant portion; (7) Round ligament.

B. (2) Pregnant interstitial portion of tube; (5) Cut end of tube; (6) Foetal membranes; (7) Round ligament.

C. (1) Placenta; (2) Excised portion of uterine cornu.

FIG. 24 A.

SECONDARY ABDOMINAL PREGNANCY.

(Specimen kindly presented by Professor Roy Dobbin.)

Lateral view. (1) Umbilicus; (2) Abdominal wall; (3) Blood-clot in the cavity of gestation sac; (4) Placenta; (5) Intestines; (6) Pubic bone; (7) Site of operation.

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FIG. 24 B.

SECONDARY ABDOMINAL PREGNANCY.

(Specimen kindly presented by Professor Roy Dobbin.)

Posterior view. (1) Placenta; (2) Intestines; (3) Fundus of uterus; (4) Cervix; (5) Vagina; (6) Blood-clot.

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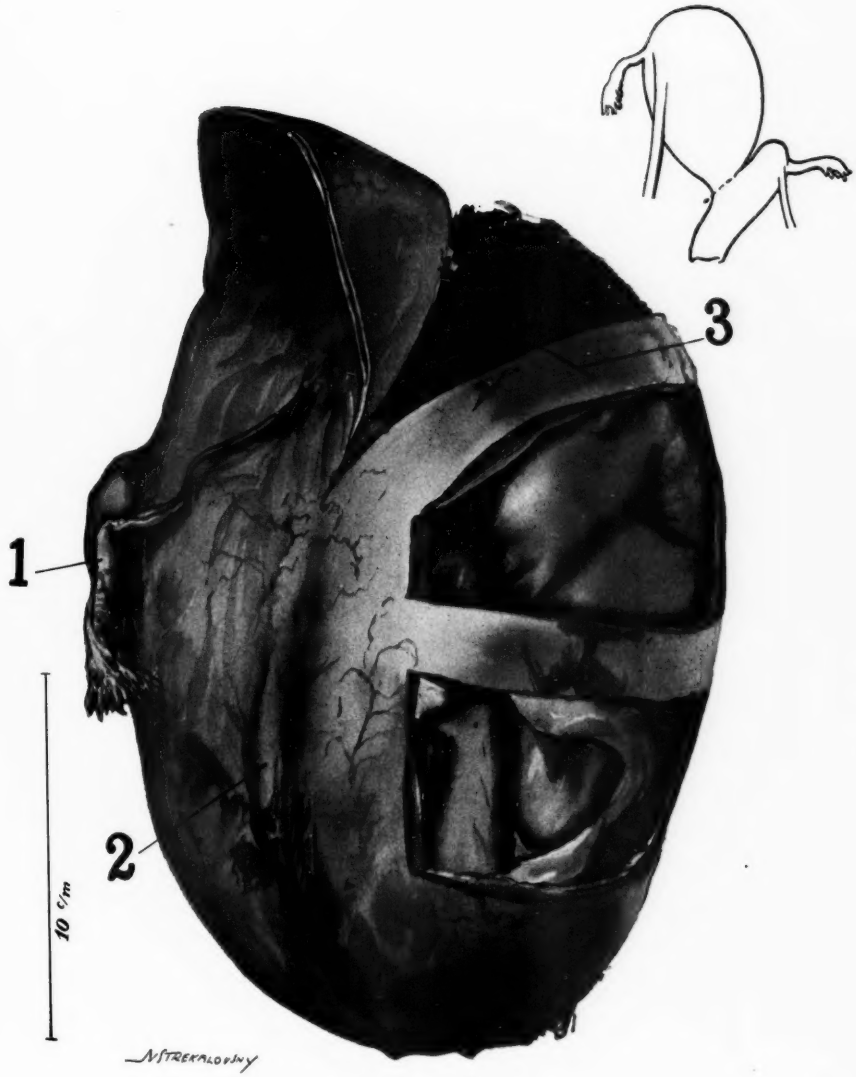

Fig. 25.

Pregnancy in the Accessory Horn of a Uterus Bicornus.

No communication was found between the pregnant horn and the cervix. Impregnation must have occurred by the external migration of a spermatozoa, and not by the migration of an impregnated ovum as the ovary of the opposite side was the seat of extensive cystic degeneration. (1) Fallopian tube; (2) Round ligament; (3) Bristle passed from the cavity of the pregnant horn along the internal opening of the tube.

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Decidual cast of the non-pregnant horn.

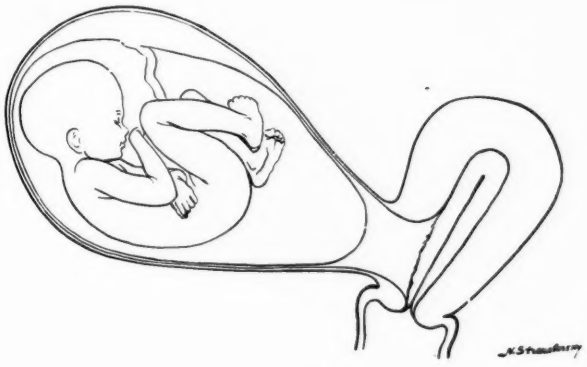

Fig. 26.

Incomplete Rupture of the Pregnant Rudimentary Horn of an Uterus Bicornus.

Diagram showing actual condition before operation.

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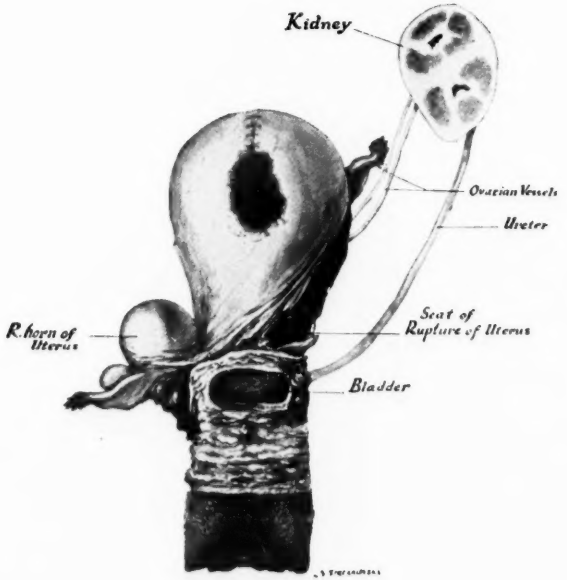

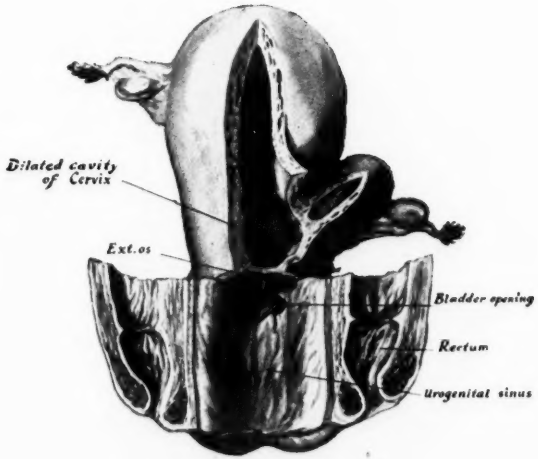

FIG. 27.

Persistence of urogenital sinus. Uterus bicornus.
Seven months' pregnancy rupture.
(Anterior Surface.)

Persistence of urogenital sinus. Uterus bicornus.
Seven months' pregnancy rupture.
(Posterior Surface.)

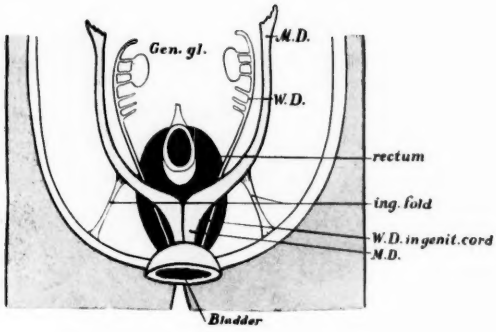

FIG. 28.

Diagram of the Müllerian ducts at the commencement of the third month. Ventral view. (Arthur Keith.)

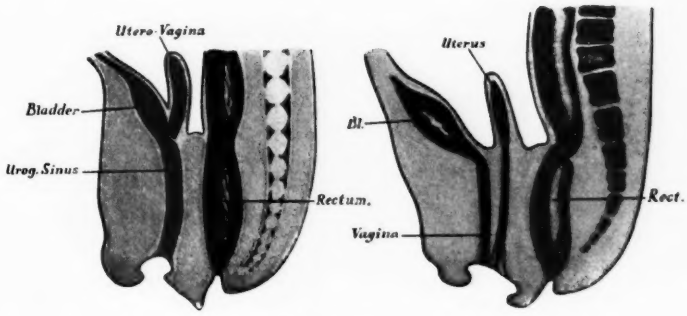

FIG. 29.

Diagram showing the termination of the vagina.

About the seventh week. About the thirteenth week.

(After Wood Jones.)

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Foetal Mortality in the Offspring of apparently Healthy Women

BY

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AIM OF INVESTIGATION.

THIS was undertaken in an attempt to discover a cause contributing to habitual abortion or stillbirths in apparently healthy women. Sterility is very disappointing to would-be parents, but it probably causes less unhappiness and disappointment than is experienced when an apparently healthy wife is able to conceive normally but is unable to carry a pregnancy to term. The latter type of patient is also a continual challenge to her doctor. We hear so much of the unwanted child, but here are patients wanting children whom we seem unable to help. On the whole these patients become pregnant as easily as their more fortunate sisters, but seem incapable of carrying their pregnancies to term.

On the supposition that frequent abortions and stillbirths may be due to some endocrine abnormality, i.e. a deficiency or excess of essential hormones, it was decided to perform a series of Aschheim-Zondek tests on the urine of some pregnant women who had previously been unable to carry a pregnancy to term, to see if their reactions differed in any recognizable way from the reaction obtained from the urine of normal pregnant patients.

The patients tested were apparently healthy pregnant women attending the Bristol Royal Infirmary, the Bristol Maternity Hospital, or were private patients.

Provided the patients appeared healthy a method of selection was not used, it was sufficient that the patient had a history of at least two previous abortions or stillbirths (with one patient a threatened abortion with severe bleeding counted as the second abortion).

By this method, as might be expected, the patients differed rather widely in social status and living conditions. However, it happened that not any of the patients investigated were really poor, that is, poor enough to lack adequate food, clothing, or ordinary comfort.

It being considered that poor general health might of itself be a cause of abortion in some cases, any patient whose general health was not good was not included.

Each patient was carefully tested to exclude syphilis, Bright's disease, or any other recognized or likely cause of abortion. In the early cases blood-counts—total red-cells, total white-cells and differential white-cells—were made during pregnancy and after abortion.

Nothing distinctive was found in these, however, so after a short time they were discontinued.

In 1933, during the course of this investigation, Dr. E. C. P. Williams[1] reported a series of cases of repeated miscarriages, 90 per cent of whom she discovered had a lowered sugar tolerance threshold.

At this time it was becoming evident that the Aschheim-Zondek reaction in the present series of pregnant habitual aborters was definitely weaker than that obtained from urine of normal pregnant patients, and it seemed worth while investigating to see if any connexion could be traced between a lowered sugar tolerance and a lowered excretion of gonadotropic hormones. Six cases were tested; with these, however, the sugar tolerance was practically normal, so, as such connexion could not be discovered, further sugar curves were not made.

Having thus excluded recognized causes of abortion or premature labour, it was decided to investigate and trace the hormone excretion by means of a series of Aschheim-Zondek reactions for each patient.

At first the urine for the test was collected by catheters, but the first morning specimen is richest in hormones, and as the patients in some instances lived at a considerable distance from hospital, this method soon produced difficulties and it became necessary at times to be satisfied with non-catheter specimens. These apparently acted just as well, so eventually catheter collections were entirely discarded.

As soon as possible after collection the specimen was sent either to hospital or the University, whichever seemed easier to the persons concerned. Occasionally specimens had to be sent by post; in every case the specimen was used as soon as possible. If a specimen arrived at the University laboratory between visits it was immediately placed in the refrigerator. "Untreated whole urine may be kept in a refrigerator for at least one year without any demonstrable loss of hormone" (Hamburger[2]).

For these experiments whole urine was used as it was felt

that treatment to the urine might result in some minor differences in the reactions. In a few cases the urine proved toxic to the mice and then resource was made to the method of detoxication used in Edinburgh (Robson[3]).

Method of Detoxication.

One gram of sulphosalicylic acid was added to 25 c.c. of urine and allowed to stand for 30 minutes with occasional shaking. It was then filtered and neutralized with bicarbonate of soda ready for use.

For the injection a sterile hypodermic syringe was used with a fine needle. (Stainless steel needles give most satisfactory results). Unless a fine needle is used the urine tends to leak back after the injection.

The early experiments were performed with graduated doses of urine from normal pregnant women in order to set up a standard of normality. Five mice and one control were used for the first five experiments, after that it was decided that a control was unnecessary.

The minimum of urine which could be depended upon to give a response with normal pregnant patients appeared to be in the region of 0.1 c.c. for 4 injections. This amount for only 3 injections was not always sufficient.

It was felt that the test would prove more delicate with smaller rather than with larger injections, therefore it was decided to give 0.1 c.c., 0.15 c.c., 0.2 c.c., 0.3 c.c., and 0.4 c.c. to allow for variations in the strengths of the various urines. These amounts were given twice daily for 4 injections.

At first autopsies were performed after various periods, but it was soon found that one could not depend on getting a definite reatcion less than 96 to 100 hours. As a definite standard was necessary it was decided to do autopsies only after 96 hours.

A mouse unit of luteinizing hormone has been described as the smallest dose able to produce corpora lutea in three out of five mice (Hamburger[4]). (The margin of error is wide).

Urine from normal pregnant patients usually gives many units per test, but in this series it was found that many sufferers from habitual abortion give reactions in which the content is less than one unit per test, and although one frequently found perfectly normal Aschheim-Zondek reactions with these patients, if a series of tests was considered, reaction II and III proved to be definitely weaker with these than with a similar series from urine of normal pregnant patients.

This agrees with the findings published by Robson,[5] who states: "It should be mentioned that occasionally when the Aschheim-Zondek reaction is negative in the presence of gestation, the latter has terminated unfavourably by abortion"; and by Crew,[6] reporting from the Edinburgh diagnosis laboratory, who says in cases of habitual abortion: "It has been found that the transformation of a positive into a weakly positive has commonly sounded a warning note." L. M. Jefferies[7] reports the case of a patient pregnant for the fourth time, the previous pregnancies all having terminated by abortion. This patient's urine was tested at frequent intervals for the Aschheim-Zondek reaction. The first test did not show any luteinization and all the reactions were weak until the fifth month when all five mice showed the reaction for the first time.

Nature is very prodigal and the gonadotropic hormone excreted in the urine is only the excess of supply over demand. This being so the margin of safety for the babies of these patients is apparently far smaller than for the babies of normal pregnant patients.

Can this margin of safety be increased?

Rationale of Treatment by Corpus Luteum.

The corpus luteum secretion, progestin, has not been recovered from any body fluid. It is, of course, secreted by the corpus luteum, but in addition it may quite possibly also be produced in the placenta (Robson[8]). It has been extracted from the placenta, and recent work seems to indicate that in some animals at least it is produced in this organ. One can imagine that this might be a function produced through the medium of the granulosa cells which surround the ovum when it leaves the ovarian follicle, for those granulosa cells remaining in the follicle later form the true corpus luteum cells.

There are well known clinical conditions and disabilities recognized as being due to under- or over-function of other ductless glands. Therefore it is easy to imagine that a corpus luteum can default in a small minority of patients in the direction of under-function, perhaps from lack of anterior pituitary stimulation (prolan) and so fail in its task of guarding the pregnancy.

Is it possible to overcome this failure?

At the Bristol Royal Infirmary corpus luteum had been given orally for many years to cases of threatened abortion by

Professor Statham, who considers it a valuable additional treatment in this condition.

The preparation used was that of Armour & Co. In a personal communication from this firm they state: "It is prepared from corpora lutea taken from pregnant sows and these glands are in course of process within one hour of the kill. . . . There is no standardization in the preparation."

It is known that treatment with corpus luteum given orally is not always successful, but very few treatments can be claimed to be 100 per cent successful and probably the failures, at any rate in part, are due to insufficient dosage.

As in many other conditions and treatments, it has been found necessary greatly to increase the dose for good results with these cases. Robson[9] states: "The failure to use sufficient doses frequently militated against the success of clinical measures with the sex hormones." Kaufmann[10] also: "In my opinion the most important principle deducible from these experiments was the fact that the doses I had found absolutely necessary . . . were far higher than any which had then been used for therapeutic purposes."

Beatrice Turner,[11] relating the results of a clinical investigation into the treatment of dysmenorrhoea in working girls by means of endocrine preparations only, states: "Endocrine preparations were given by mouth . . . the group of girls with pain after the onset and a more copious flow received 5 grains of corpus luteum twice daily. Contrary to current belief this had undoubtedly been absorbed in a few cases with dramatic effect."

Many people confidently state that corpus luteum given orally has no effect whatever. This is a similar statement to the one so frequently used about ergot until a short time ago when Moir and Dudley[12] published their researches giving an account of ergometrine, thus vindicating the many doctors up and down the country who, judging by the results only, had continued to use orally the watery extract of ergot, although they had been informed so many times that this had been proved to be inert.

Direct Corpus Luteum Feeding to Mice.

To try to clear up this point a series of tests was performed by feeding mice with corpus luteum. The mice were 3 weeks old at the time the tests were started and the tablets of corpus luteum (Armour's) the same as those with which the pregnant patients were being treated. Nine mice were given varying doses of corpus luteum, the largest being 3 grains daily. The mice were

autopsied on different days, the last one after 10 days' feeding with corpus luteum. On examination the ovaries of these mice did not differ in any essential way from the ovary of a normal control mouse, either macroscopically or microscopically.

Being convinced by clinical experience that the pregnant patients under investigation were deriving benefit from the tablets, it seemed possible that they were being sensitized by some other factor. The follicle stimulating hormone is present in large amounts in pregnancy, producing oestrin. Therefore, it was decided to try to sensitize the mice by injecting oestrin. Progynon was the preparation used. Later this was found to be in accordance with Robson's statement: "The corpus luteum hormone is, however, unable to exert its action in the absence of oestrin." [13]

Six mice were injected with 2 mouse units of progynon twice daily for 2 days and then given corpus luteum 2 grains daily. After 5 days on corpus luteum 2 mice were killed and examined post-mortem. These showed a mild degree of uterine enlargement and one showed one point thought to be corpus luteum by naked-eye examination. Next day the remaining 4 mice were killed and examined. Macroscopically these showed mild ovarian enlargement but nothing more definite.

On microscopical section, however, it was evident that follicles had been stimulated and some of them showed commencing luteinization and even minor haemorrhages. (See Fig. 1). This was thought to be due to the corpus luteum feeding as progynon, i.e. oestrin or the follicular hormone was believed to have no effect on the ovaries. "It (oestrin) has no stimulating effect on the ovaries. There is some evidence that it can inhibit follicular development" (Cameron[14]). However, Hohlweg, in a lecture at Milan before the Italian Congress for Gynaecology and Obstetrics (1937) claims that corpora lutea are found in the ovaries of immature rats treated with oestrin.

These experiments, therefore, on direct corpus luteum feeding to mice did not appear very decisive, and if it had not been for the previous experience with the tablets of corpus luteum given orally, it is probable that one of the anterior pituitary preparations would have been used as soon as the weak reactions were discovered, or even the extract of corpus luteum by hypodermic injections might have been considered.

However, it was considered that the above tablets were satisfactory in use and worthy of a more definite trial. The results have justified the experiment.

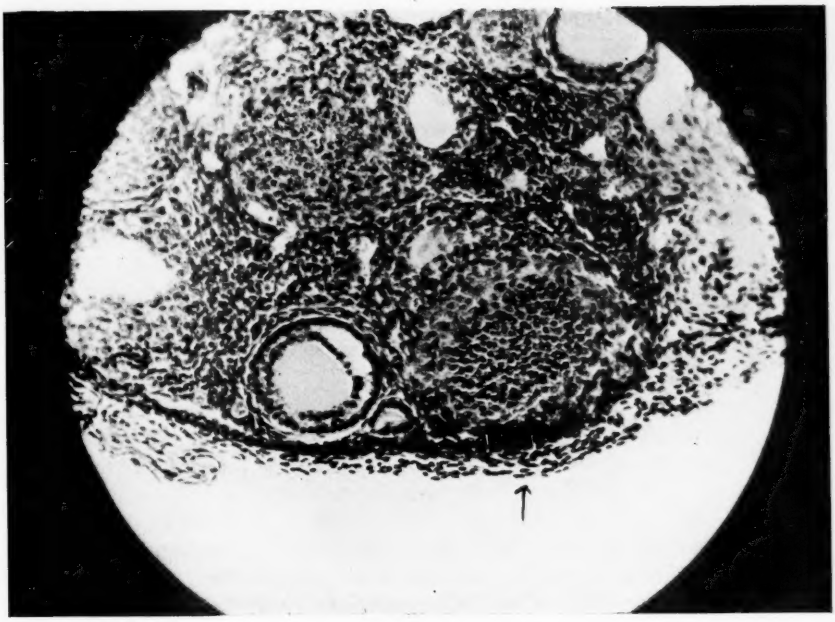

FIG. 1.

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During the course of this investigation it has frequently been noticed that labour has to be induced when patients are taking large doses of corpus luteum, as the pregnancies tend to become post-mature.

Aschheim-Zondek Results.

Up to December 1936 urines from 260 different normal patients or from subjects of persistent abortion were injected into mice and the results noted.

Autopsies for this purpose have been performed on about 1,800 mice.

It was early noticed that although the urine of pregnant women who produced stillbirths and abortions very frequently gave perfectly normal Aschheim-Zondek reactions, if a series of tests was performed, the results were definitely weaker than those with the urines of normal pregnant patients.

On many patients only one test was done but numerous tests have been performed on those patients who, being pregnant, give a history of previous stillbirths and abortions and also on a certain number of normal pregnant patients as controls.

In an endeavour to estimate the strength of the Aschheim-Zondek reaction in this series only ovaries showing haemorrhages were considered at first, but there is much more in the reaction than that, so later a record was made of uterine enlargement, ovarian haemorrhages, presence of corpus luteum and even mere ovarian enlargement, this latter usually being accompanied by marked hyperaemia.

The clinical histories of the controls were entirely uneventful except for one case. This patient, E.M., aged 30 years, gave a history of three previous pregnancies and labours which appeared perfectly normal. The babies weighed 9 pounds, 8 pounds, and 8 pounds respectively. She seemed the ideal patient for a control. It was very disappointing, therefore, to find that unlike all the other controls this apparently normal patient was giving very weak reactions which approximated closely to those given by the sufferers from habitual abortion. On three occasions at 13 weeks, 20 weeks, and 27 weeks, her reactions were negative. It was not considered necessary to treat this patient, there not being any reason to think that this pregnancy was different in any way or that it would end differently from her others. At 24 weeks, however, the membranes ruptured spontaneously while she was walking with her children. She was admitted to hospital and was kept in bed for 8 days. After this she was discharged but

continued to lose liquor amnii. The uterus increased in size, however, and the foetal heart was heard. At 30 weeks labour began, the baby was feeble, it weighed only 5 pounds, and died in 6 hours. The unhappy ending of this pregnancy at 30 weeks seems to indicate that a pregnancy cannot be considered safe if the mother's urine gives such a series of weak or negative Aschheim-Zondek reactions.

It is difficult to understand, however, why this apparently normal patient should have three normal pregnancies and then suffer from a deficiency of gonadotropic hormone and lose her fourth pregnancy.

Habitual Aborters.

There were 19 patients in this series of habitual stillbirth and abortion patients. They all gave weaker Aschheim-Zondek reactions than those given by normal control patients; in many cases they were much weaker, in several cases being negative during most of the pregnancy. All these patients were placed on corpus luteum treatment.

Three Failures.

Three of these cases ended in failure. Of these, two had living babies with their first pregnancies followed by an abortion prior to the one for which they were treated. The first of these failures gave a very weak reaction in her first test. One mouse in five showed haemorrhage but of the other tests some showed ovarian enlargement and even corpora lutea in the test ovaries but haemorrhage was not present. Labour began in this case at the thirty-seventh week and a son weighing $5\frac{1}{4}$ pounds was born. Breast milk was not available and the baby had to be artificially fed. He gradually lost weight and died in 2 weeks. Diarrhoea and vomiting were present for 2 days before death.

The premature birth of this baby was almost certainly due to lack of experience at this stage. The patient needed much larger doses of corpus luteum, she never had more than 4 grains *per diem*, partly because of the expense and partly because at this early stage we were not giving the larger doses later considered necessary.

This was the second patient giving these weak Aschheim-Zondek reactions who also suffered from poor mammary secretions. Had this baby been able to have the inestimable advantage of breast milk it would have had a much better chance of surviving in spite of its premature birth, for it made no headway

on artificial feeding and eventually died from an infection which is extremely rare in a breast-fed baby.

The second failure was in a patient who gave several indications of hormone deficiency, (1) obesity, (2) irregular and scanty menstruation, (3) infrequent but greatly desired pregnancies.

She was given corpus luteum 2 grains three times daily when first seen at 18 weeks. At 24 weeks this was reduced to 2 grains twice daily, as she had passed the date of her previous miscarriages. This was a mistake, however, in view of her Aschheim-Zondek reactions, which indicated a need of greater corpus luteum dosage, which, of course, was further demonstrated by her inability to carry on the pregnancy.

The third and last failure was 8 weeks pregnant when first seen. She gave a history of premature stillbirth followed by 2 abortions at the fourth month. She was given 2 grains of corpus luteum twice daily and was a further demonstration of the futility of this small dosage. After this we depended only on the larger doses, several patients having 18 grains daily.

Threatened Abortions.

There were six interesting cases of threatened abortion in this series, in each of which the pregnancy was preserved.

Case A.M.M., No. 23. She was eight weeks pregnant when abortion threatened. This patient first aborted at nine weeks in August 1932, when a diagnosis of ectopic gestation was made. At the operation, however, no such lesion was found. In spite of careful search neither ovary—both of which were cystic—showed the presence of a corpus luteum, and it was thought that this contributed in some measure to the abortion.

This patient again became pregnant in July 1933, and aborted before the third month. Tests were made on two occasions to exclude syphilis or a pathological renal condition.

In November 1933 she again aborted, and was advised to report for corpus luteum treatment as soon as she again became pregnant. She was placed on corpus luteum, 2 grains three times daily, when she next reported, which was before her second period was missed. Her Aschheim-Zondek reaction fluctuated greatly. At 26 weeks it was almost negative. This was followed at 28 weeks by pain and vaginal bleeding. At once her corpus luteum was increased to 18 grains daily, which appeared to stop the bleeding. This pregnancy ended in the birth of a healthy baby girl, her first living child born 10 months and 1 week after her third abortion.

One cannot help wondering why this patient apparently had no luteal body during her first pregnancy. Had it atrophied? Was she lacking in gonadotropic hormone, and so in luteal

hormone? Did the corpus-luteum feeding enable the pregnancy to continue? These questions are difficult to answer, but we know this patient's excretion of gonadotropic hormone had fallen exceedingly low one week before the bleeding started. Massive doses of corpus luteum were given, the bleeding ceased, the Aschheim-Zondek reactions became stronger, and the patient carried on to term.

Case C.P., No. 46, threatened to abort. She had one living child, born in 1931. She miscarried at 6 months in June 1934. Abortion threatened at 2 months; was in hospital until bleeding ceased. On discharge, however, bleeding recommenced, the loss being marked by numerous clots. Patient said it was impossible to enter the hospital again, but she would rest as much as possible at home. She was given corpus luteum, 12 grains daily. At 13 weeks there was still some bleeding so the corpus luteum was increased to 18 grains daily. The bleeding then ceased.

This patient had a husband, and a child 3 years of age. She managed the housework, washing and meals for all with occasional help from her mother and, therefore, could not stay in bed even when the bleeding was severe. She really wanted to preserve the pregnancy and was willing to take any medicine she thought would help and on two occasions walked to hospital for fresh supplies of tablets even when one felt rest in bed would probably have been more useful in her case. She considered, however, she was better with tablets even with exercise rather than with rest but without tablets.

She managed to save the pregnancy and had a normal living baby girl at term.

Case M.T., No. 47, threatened to abort. She had been married 2 years. She aborted at the third month in July 1933, and at the tenth week in January 1934. When first seen she was 11 to 12 weeks' pregnant and losing blood *per vaginam*.

This patient, her husband and the family doctor were determined to do all that was possible to preserve the second pregnancy, but in spite of their utmost care, she aborted. When she started bleeding at about the same period in her third pregnancy, there seemed nothing further they could do, so further advice was sought. The only additional treatment prescribed were large doses of corpus luteum. The bleeding ceased with this and the patient was able to carry on the pregnancy to term.

Case M.M., No. 173. She had three normal labours 16, 11 and 6 years ago, then 3 abortions, the first at 3 months, the second and third at 4 months. When she was threatening to abort at the fourth month she was sent home to bed and given large doses of corpus luteum and also calcium lactate 5 grains three times daily. Pain and bleeding ceased but there was slight bleeding again at 26 weeks which lasted a fortnight, but was unaccompanied by pain. All the Aschheim-Zondek reactions were weak, but in spite of this the patient had a normal living baby at 39 weeks.

Case E.T., No. 2264, threatened to abort. She had been married for 9 years. One premature stillbirth had occurred at the seventh month, and one miscarriage at the third month. She was 2 months' pregnant and complaining of pain and bleeding.

She became pregnant only at infrequent intervals and it seems as if each pregnancy was terminating earlier than the previous one. She was given at once large doses of corpus luteum and sent home to bed until bleeding had ceased for a week. She continued taking corpus luteum until 33 weeks and took it again for 2 weeks at about 8 months.

This patient came into labour at term and was delivered by the forceps of a living baby weighing 8½ pounds.

Case F.C., aged 29 years, threatened to abort. Aschheim-Zondek tests were not performed for this patient. Her case is included, however, because after 2 failures and in spite of a threatened abortion she responded to treatment with corpus lutuem and had a living baby, but failed again in a subsequent pregnancy for which she did not receive any treatment. In October 1933, macerated foetus. In October 1934, abortion occurred at the second month. Abortion was threatening when she was first seen at the sixth week of her third pregnancy. She was given corpus luteum and ostelin orally from 6 weeks until term. In June 1936 a normal living baby, weighing 7½ pounds, was born. She again became pregnant in May 1937, and aborted at the second month. The patient had not received any treatment for she had not realized she was again pregnant until excessive bleeding started.

Résumé of Results.

This series of cases of habitual stillbirths and abortions gives a high percentage of pregnancies successfully terminated, especially compared with what the same patients were able to accomplish unaided by corpus luteum.

Without this treatment 19 patients had between them 55 pregnancies. Of these only 8 were successful and 47 ended in failure.

These same 19 patients, however, under treatment with corpus luteum achieved success with 16 pregnancies and failed only in 3.

Table I.

19 *patients*.

	Pregnancies	Failures	Successes
Without corpus luteum	55	47=85.4 per cent	8=14.5 per cent
With corpus luteum ...	19	3=16 ,,	16=84 ,,

As will be seen by this table the percentage of successes

and failures is practically reversed with treatment in this small number of cases.

This result is particularly gratifying with the 6 patients who responded to the treatment in spite of a threatened abortion and were thus enabled to have a living child at term.

Tables II and III give the Aschheim-Zondek reactions of these patients totalled and compared with the series of controls. For greater accuracy the individual mice have been counted.

TABLE II.

Results of injection of urines from patients in first half of pregnancy.

Controls (340 mice used).	Positive No.	Positive Per cent	Aborters (180 mice used).	Positive No.	Positive Per cent
Uteri (340)	320	91	Uteri (180)	171	95
Ovaries (680)—			Ovaries (360)—		
With haemorrhage ...	342	50	With haemorrhage ...	137	38
With corpus luteum ...	459	67.5	With corpus luteum ...	209	58
With enlargement ...	554	81	With enlargement ...	241	65

TABLE III.

Results of injection of urine from patients 20 to 40 weeks pregnant.

Controls (213 mice used).	Positive No.	Positive Per cent	Aborters (327 mice used).	Positive No.	Positive Per cent
Uteri (213)	204	95	Uteri (327)	308	94
Ovaries (426)—			Ovaries (684)—		
With haemorrhage ...	132	31	With haemorrhage ...	116	17.7
With corpus luteum ...	260	61	With corpus luteum...	248	38
With enlargement ...	307	72	With enlargement ...	328	50

As may be seen on reference to Tables II and III uterine enlargement in the test mice, the reaction 1 of the Aschheim-Zondek test due to the presence of oestrin and of prolan A in the injected urines, was fairly constant in this series of controls and abortion patients.

This also proves true when various degrees of enlargement are taken as a standard, for in each type of patient the results are nearly equal (15).

However, the remainder of the test, reaction 2 and 3, in the

two types of patient is considerably different, the habitual abortion patients generally showing much weaker reactions, although they frequently give a perfectly normal reaction at some stage or stages of their pregnancies, suggesting probably that their endocrine balance is unstable and inconstant.

Aschheim-Zondek Reaction at Term on Normal Pregnant Patients Treated by Induction.

In this present investigation we have in every case endeavoured to preserve the pregnancy. In other cases such as cases of slight disproportion it is sometimes necessary to induce labour.

It is a well known fact that at full term a medical induction acts quickly and easily in a large proportion of cases, but in others difficulty is experienced, the attempt at medical induction fails, and something has to be carried out surgically.

If the ease or difficulty of inducing labour depends on the hormone balance of the mother it seemed as if this might show in the hormone content of the urine. Therefore, Aschheim-Zondek tests were performed on the urines of 24 normal primiparous patients in whom it was considered necessary to induce labour at term in order to avoid disproportion due to the size of the pelvis or baby or in view of the patient's age.

Of these 24 cases, 17 responded and 7 cases failed, there being in the latter no sign of labour 36 hours after the medical induction had been started. Contrary to expectation the patients who gave the weaker reactions were those who failed to respond to the induction.

The Aschheim-Zondek results in 17 cases which responded to medical induction were as follows: Reaction 1: uterine enlargement; 92 per cent showed enlargement. Reaction 2 and 3, ovarian 20 per cent showed haemorrhages, 26 per cent showed corpora lutea, and 55 per cent were enlarged and hyperaemic.

The Aschheim-Zondek results in 7 patients who failed to respond to medical induction were as follows: Reaction 1: uterine enlargement; 57 per cent showed enlargement. Reaction 2 and 3, ovarian: 9 per cent showed haemorrhages, 10.6 per cent showed corpora lutea, and 16 per cent were enlarged and hyperaemic.

It is difficult to understand these results obtained from perfectly healthy normal patients. Of course, they were obtained from excretion products contained in urine. It may be that the patients who responded to the induction and gave the stronger

reactions were excreting a larger proportion of the hormones, while the patients who failed to respond gave weaker reactions because they were utilizing all the available hormones and, therefore, had less to excrete.

This result is the opposite to that obtained in the habitual abortion patient, for the latter patient gives a weak reaction and is unable to preserve a pregnancy.

It may be that there is another as yet undiscovered hormone, or other factor helping to control the uterus, and thus making it safe for the ovum or foetus.

This investigation on persistent abortion patients indicates that with a weak Aschheim-Zondek reaction the pregnancy is insecure. This other factor, however, may run more or less parallel with the urinary hormones but does not give any macroscopic or microscopic indication of its presence; it might even prove to be a chemical factor.

Young,[16] in an article "Habitual Abortion and Stillbirth Syndrome," gives a similar series of habitual abortion patients to that presented here. He suggests that the evidence "is consistent with the view that an important cause of habitual abortion . . . is a disturbance in the metabolism of pregnancy in which a deficiency of vitamin B is involved." He also "raises the question as to the part which vitamin E plays in the prolan progesterone mechanism of pregnancy."

Young states "that the available data are consistent with the view that vitamin E possesses specific significance for the nutrition of the placenta and that, in some manner which is not clear, it operates through the activation of the luteinizing mechanism."

Working on the theory of a deficient luteinizing mechanism, Young treated 17 patients with prolan who before treatment had between them 51 successive pregnancies which had all ended in abortion, but under treatment he was able to report 88.2 per cent of successes.

Pregnancies in patients who habitually abort have also been preserved by the injection of corpus luteum secretion itself, and Kaufmann,[10] by injection of oestrin and progesterone, has been able to cause to grow in women, whose ovaries had been removed, an endometrium which approximates so closely to a pre-gravid endometrium that it is impossible to detect any difference either by macroscopic or microscopic examination.

Whether this endometrium contains the essential factors necessary for successful nidation of the ovum we have no method of discovering.

Kaufmann has been unable to obtain his results on the endometrium by oral administration of oestrin and progesterone to women whose ovaries had been removed, injection being necessary in each case, but the habitual abortion patient is quite different from a woman who has had her ovaries removed. The one is suffering from complete absence of ovarian hormones, while the other is supposedly suffering merely from a deficiency, certainly not from a complete absence of the hormones.

A corpus luteum has two kinds of cells, ordinary lutein cells developed from the granulosa cells, and theca cells from the theca interna. It might be that only the one variety is concerned with stimulating the secretion of the endometrial glands and producing the ordinary pre-gravid picture, whether the paralutein or theca lutein cells "subserve any secretory function has not yet been determined" (Robson[17]).

It might be that they produce the unknown factor which we are unable to discover. Fremery, Lucks and Tausk[18] describe a hormone derived from the corpus luteum which is responsible for an inhibitory reaction on the uterus; they call it desensin. This might prove to be the unknown factor, and should it remain potent given orally, this would explain the successes shown in the present series. Perhaps the vitamin E functions through the corpus luteum in this way and not by producing any recognizable change in the structure of the endometrium.

It is difficult without some theory of this kind to understand how corpus luteum given orally helps these people.

In the feeding experiments in rats and mice a change definitely due to corpus luteum could not be detected, and in this series of cases, although the pregnancies were preserved and the reactions in some cases greatly improved, in other cases they remained weak or negative, even in patients whose pregnancies were post-mature and needed surgical interference before labour started.

Summary.

An attempt has been made to discover if possible a cause of the foetal mortality in the offspring of apparently healthy mothers.

Aschheim-Zondek reactions were performed at intervals on a group of apparently healthy pregnant patients who habitually aborted and also on a similar group of normal healthy pregnant patients to act as controls.

It was discovered that healthy patients who habitually abort, or whose children are stillborn, give weak reactions 2 and 3 in

the Aschheim-Zondek test, but their excretion of oestrin and prolan A are within normal limits, as shown by reaction 1.

An apparently healthy mother used as a control because previously she had had three healthy children at term, appeared to spoil the series; she gave similar weak reactions during her fourth pregnancy. This pregnancy, however, terminated prematurely and unsuccessfully at 30 weeks.

Attempts were made to reduce the foetal mortality in this group by treatment with corpus luteum given orally. This was found to be successful if massive doses were given.

It is suggested that the factor in the corpus luteum responsible for these successes is probably different from the factor responsible for the structural changes of the endometrium preparatory to pregnancy.

The functions of the theca lutein cells are still unknown, and it is further suggested that these theca lutein cells produce the hormone which inhibits uterine contractions and which probably remains potent if given orally.

Details are given of 19 patients who were habitual aborters.

The 19 patients had a total of 55 pregnancies prior to treatment, of which only 8 were successfully terminated, a percentage of 14.5.

On treatment with corpus luteum these same 19 patients were able to terminate successfully 16 pregnancies, giving 84 per cent successes.

Six of these successes were cases of threatened abortion which responded to corpus luteum treatment.

One of these successfully treated cases of threatened abortion occurred in a patient who failed in two previous pregnancies and again aborted in a subsequent pregnancy for which she had obtained no treatment.

Conclusions.

(1) Aschheim-Zondek reactions on a series of apparently healthy pregnant patients who habitually abort or whose children are stillborn were definitely weaker than the reactions obtained from the urine of a similar series of normal pregnant patients.

(2) The oral administration of large doses of corpus luteum to those women who habitually abort greatly increases their chance of a successful termination to a pregnancy.

I should like to record my thanks to Professor Statham, at whose instigation this investigation was undertaken, and to Professor Drew-Smythe, Professor Hadfield, and Dr. Dorothy Woodman for helpful criticism and advice.

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A very large Ovarian Cyst removed by Enucleating it from the Ovary ("Ovarian Cystectomy")

BY

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THE fact that almost all innocent ovarian cysts can be enucleated from the ovary seemed to have escaped notice until I drew attention to it in 1928; at least I do not know of any earlier mention.[1]

The case with which this communication is concerned was a woman aged 43 years who had an ovarian cyst reaching to an inch from her ensiform cartilage. On opening her abdomen I found that the cyst was in the right ovary and that the left ovary was practically non-existent and, therefore, to save her from an operative climacteric I enucleated the cyst, which weighed 14 pounds, instead of performing ovariotomy. (Fig. 1). I have enucleated ovarian cysts of various sizes a great many times, and last year published the results of these operations,[2] but this cyst was by far the largest of any that I have dealt with in this manner, and the case evokes certain interesting considerations.

A cyst as it grows in the ovary expands the ovarian substance over it just as a fibroid expands the uterine wall over it, and in either case what is left behind after the tumour has been enucleated is the whole organ. The fact that menstruation commonly persists even when both ovaries have been converted into cysts of great magnitude is, therefore, not surprising: the ovarian substance, though thinned perhaps to the thickness of parchment, is there in its entirety.

But the analogy with fibroids is closer still, for just as the uterus expanded by a fibroid hypertrophies as it expands, so the ovary expanded by a cyst hypertrophies as it expands. This, which is not noticeable when the cyst enucleated is comparatively small, is exceedingly obvious when it is very large, for the surgeon, having sutured the greatly expanded capsule into

CYST, WEIGHING 14 POUNDS, REMOVED BY ENUCLEATING IT FROM THE OVARY.

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something approaching the normal shape and consistence of the ovary, finds that the organ he has reconstructed is treble or quadruple the natural size. When the excess of capsule is considerable, part of it can be cut away before the suturing is commenced, but I have frequently returned to the abdomen without ill effects an ovary much larger than normal. Probably involution occurs just as it does after myomectomy.

As regards the technique of the operation the incision through the ovarian capsule should not be more than 2 or 3 inches to begin with and should be made by the mere weight of the scalpel lest the cyst be opened. The handle of the scalpel should then be used to separate the capsule from the cyst wall which lies beneath it. When sufficient room has been obtained, the index fingers should be inserted and the separation gently continued. while from time to time the incision in the capsule is extended until at last the whole cyst rolls out of its bed. For buckling up the capsule I use a continuous backward and forward catgut suture, and before beginning the enucleation I place a ring forceps temporarily across the hilum to render the proceedings bloodless. If the cyst be opened, either by accident or, as sometimes happens, because its wall is exceedingly thin, the cyst cavity should be opened, its contents evacuated and the cyst wall eviscerated by stripping it out.

What name should be given to the operation of enucleating an ovarian cyst? Ovariotomy expresses the nature of the proceeding for the ovary is merely cut, but custom has attached the word to the operation that removes the cyst and the ovary together. I, therefore, suggest "Ovarian Cystectomy."

I am indebted to Sir Frederick Menzies, Chief Medical Officer London County Council, for permission to record this case.

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Enucleation of Bilateral Ovarian Cysts from a young Nullipara

BY

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A YOUNG unmarried woman, 24 years of age, complained of a gradual increase in the size of her abdomen, which had recently become painful on the right side. The patient had missed two periods, but had commenced to bleed when seen at hospital. On examination a large tumour about the size of a 7 months' pregnancy was found to occupy the abdomen. Vaginal examination revealed a small uterus lying below the abdominal tumour. An X-ray photograph showed the presence of a tooth in the tumour, and the diagnosis of a dermoid cyst was made. Because of the size of the tumour, in the absence of any history of torsion, it was thought that the dermoid tumour was probably combined with a pseudomucinous cyst.

On the 12th January I opened the abdomen and discovered the large ovarian tumour to have its origin on the left side. The incision was enlarged, the intestines were packed off, and the tumour was delivered. Its dimensions were, roughly, 10 inches by 8 inches. A clamp was temporarily placed on the pedicle of the tumour and, at a point near its summit, a very superficial incision was made into the tumour. The capsule was gently separated from the wall of the cyst by the handle of the knife, and then further room was obtained by insinuating the index fingers. The cyst wall was gradually separated in a circumferential fashion. Owing to the extreme thinning of the cyst in some parts, one or two loculi were entered. Eventually the whole cyst was removed. It was found to consist of two parts, the larger one being a multilocular cystadenoma, and the smaller one a typical dermoid cyst. The redundant ovarian tissue forming the capsule of the cyst was trimmed and folded over and sutured together to form a fairly large mass, 4 inches long

by 1 inch thick. Care was taken to keep the hypertrophied Fallopian tube in a correct anatomical relation to the reconstructed ovary. On the right side the ovary was the seat of a unilocular cyst the size of an orange. The cyst was incised and the lining membrane easily dissected out. The ovary was then repaired with fine catgut. The patient has made a good recovery and has had a normal menstrual period.

The combination of a pseudomucinous cystadenoma with a dermoid cyst is relatively frequent, and occurred in 3 per cent of cases reported by Wilfrid Shaw.[1] The small cyst on the right side was a simple serous cyst.

This case reveals the ease with which the ovary may be conserved even when converted into a large ovarian tumour, an invaluable procedure when dealing with a young woman.

I am indebted to Sir Frederick Menzies, Chief Medical Officer, L.C.C., for permission to record this case.

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Gynandroblastoma of the Ovary

BY

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ON the so-called germinal epithelium blastomata of the ovary many papers have already been published. Nevertheless, the study of these tumours may yield aspects which undoubtedly deserve special consideration. This is certainly true for the gynandroblastoma, which is a combination of granulosa-cell tumour and arrhenoblastoma. In the Gynaecological Clinic, Amsterdam, a growth of this kind was removed and examined.

Mrs. D. (Case No. 10767), 26 years of age, was admitted to the hospital on October 18th, 1937. Her main trouble was disturbance of menstruation. Until February 1935 the periods, which had begun at the age of 14, had been regular, with a cycle of 28 to 30 days and a duration of 5 days. In that year periods of amenorrhoea occurred, lasting 4 to 5 months and ending with a haemorrhage which was more severe and of a longer duration than a normal period. In June 1935 she had a continuous loss for 20 days. The last menstruation occurred in November 1936. Since February 1935 growth of hair has appeared on the face and the voice has become deeper. Sometimes she is troubled by flushing, and she thinks she has become more nervous than before. She is married, but she has never been pregnant.

On examination she was found to be well nourished. On the face there was a slight growth of moustache and beard, the mammae were well developed, and the hair on the abdomen was of a virile type. The voice was conspicuously deep. Signs of pregnancy were absent: there was not any colostrum, pigmentation, or lividity of the vaginal mucosa. The clitoris and vagina were normal. The body of the uterus was in anteflexion, it was normal in size and consistence, and was somewhat displaced to the right by a rather firm lump in the left half of the pelvis.

The patient was operated upon on October 21st. The left ovary presented as a solid growth the size of a large tangerine orange. The right ovary was normal. The growth was removed with the lateral portion of the left Fallopian tube, and the appendix was removed.

The post-operative course was undisturbed, and the patient was discharged on November 4th in a good condition. On December 3rd she attended for examination and reported that she had menstruated normally from November 21st to 26th. The amount of hair on the face had diminished, but on the abdomen it was still unchanged; the voice was still deep. On examination no other abnormal condition was found in the pelvis.

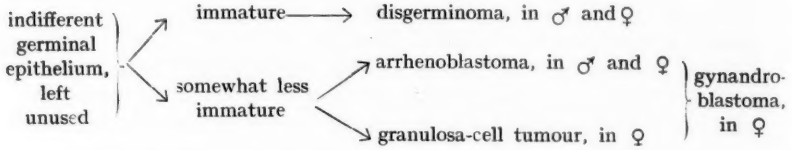
The ovarian tumour was yellow on section. The largest part was occupied by a cavity filled with a coagulated mass of a clear yellow colour. On the other pole a structure the size of a cherry was found which resembles a corpus luteum. Between the cavity and this portion there were islets of tissue of an intense yellow colour. Fig. 1 is a diagram of the appearance of the growth, in which, in addition, the parts which have been sectioned for microscopy are indicated. In section I, in a slightly oedematous stroma, strands and islets of cells are seen having the appearance of granulosa cells. In the islets in many places a folliculoid structure can be strikingly seen (Fig. 2). Section II shows a preponderance of the adenoma picture: tubules coated with a low cylindrical epithelium (Fig. 3). The cavity is coated with a layer of cells resembling granulosa cells, and in its neighbourhood strands of the same cells are seen. The solid strands merge gradually into the tubules (Fig. 4). Section III shows both constituents of the tumour along with each other. In Fig. 5 one sees above a *moiré* pattern typical for granulosa-cell tumour, and below the tubules characteristic of arrhenoblastoma. The adenomatous portion corresponds with the patches of an intense yellow colour seen macroscopically on the cutting surface.

In the growth elements of granulosa-cell tumour and of arrhenoblastoma were found. In Fig. 5 these components are seen completely separated from each other, but in Fig. 4 a gradual transition is visible. The qualification of gynandroblastoma is, therefore, justified. In this case one can expect symptoms characteristic for granulosa-cell tumour or for arrhenoblastoma, which will depend on which of the components preponderates in hormonal action. The history and signs of this

patient made one expect an arrhenoblastoma, the deep voice and the growth of hair on the face and abdomen pointing in this direction. These signs are certainly not compatible with a granulosa-cell tumour. Amenorrhoea may occur in the presence of either kind of tumour, in the case of arrhenoblastoma being a sign of defeminization, whereas in granulosa-cell tumour it is caused either by excessive production of folliculin (with hyperplasia of the uterine mucosa and temporary amenorrhoea, alternating with haemorrhages), or by luteinization of the tumour (causing pseudo-pregnancy). The restoration of the menstrual function after the removal of the tumour shows clearly that the phenomenon was caused by the tumour. We were interested to know the condition of the endometrium and, therefore, removed some tissue from the cavum uteri with a suction curette on October 20th and 28th. The material of the first removal, unfortunately, was not sufficient for microscopical examination; that of October 28th showed an almost normal mucous membrane with a few ectatic glands, certainly not deserving the name of typical hyperplasia.

So far as we could find in the literature on blastoma of the germinal epithelium, 12 gynandroblastomata have been described, viz.: by Meyer,[1] Tietze,[2] Amati,[3] Schiller,[4] Eerland and Vos,[5] and Frankl.[6] Nine out of these 12 patients were in the period of active sexual function, the other three (Tietze's cases) were at the menopause. Kehrer[7] mentions gynandroblastoma and observes that it is still hypothetical. Descriptions of this kind of tumour can be found in papers on arrhenoblastoma and in those on so-called masculinizing granulosa-cell tumours. In our opinion a pure granulosa-cell tumour cannot cause masculinization. The neoplasms known as luteinized granulosa-cell tumours with virilism are hypernephromata, as Schiller[8] has clearly shown. The other granulosa-cell tumours with signs of masculinization must contain elements belonging to arrhenoblastoma, and are, therefore, gynandroblastomata.

The histogenesis of the blastomata of the germinal epithelium is indicated by the following diagram:—



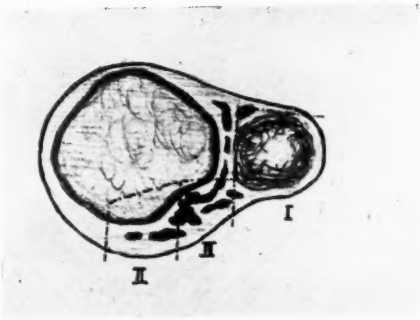


FIG. 1.
Diagram of tumour in section.

FIG. 2. SECTION I.
Folliculoid structure of tumour.

FIG. 3. SECTION II.
Adenomatous structure of tumour.

FIG. 4. SECTION II.
Above, to the right: cavity, coated with granulosa cells; below this strands of these cells. Middle: tubules.

FIG. 5. SECTION III.
Above: "moiré" pattern. Below: tubules.

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Arrhenoblastoma and granulosa-cell tumours arise from epithelium of the same degree of maturation, and it is not illogical that elements of both kinds of tumours should occur together in one growth, the gynandroblastoma; the indifferent germinal epithelium develops partly in the male and partly in the female direction. Amati, in his tumour, found, side-to-side with adenomatous portions (arrhenoblastoma) and parts resembling Graafian follicles (granulosa-cell tumour), also elements which he thinks justified his calling large-cell carcinoma (disgerminoma). This would be the first case of blastoma of the germinal epithelium containing all three elements.

The gynandroblastoma, as the other blastomata of the germinal epithelium, can show malignant degeneration. Meyer, in his case, assumes the diagnosis of carcinoma on the microscopical appearance; Eerland and Vos are in doubt whether their third case is malignant. Undoubtedly malignant is the first case of Schiller, as has been proved later by Hückel.[9] In our case the histological picture is benign.

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The Seminoma or Dysgerminoma of the Ovary

BY

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THE tumour discussed in this paper has been variously designated seminoma and dysgerminoma. The term "seminoma" has been condemned by Meyer,[1, 2, 3] who first suggested the latter term to replace it, but it may be retained on the grounds of simplicity, since the tumour, as it occurs in the ovary, closely resembles its better-known namesake in the testis.

The seminoma ovarii is of moderate rarity among solid ovarian tumours, and the author was able to collect only 8 cases from the records and pathological specimens of the the last 30 years in University College Hospital Medical School, including one case originally under the care of Mr. Dudley Buxton in King's College Hospital, and included in this series with his kind permission. All ovarian tumours in which the pathological diagnosis was uncertain, especially those labelled "sarcoma", were subjected to close scrutiny, as well as tumours from patients with abnormal sexual development, such as Case 1. So far as possible, all museum specimens were resectioned, often with surprisingly good results, despite preservation in some instances for 10 years or more in spirit.

In one instance data on the case were so inadequate that it has been excluded. The remaining 7 cases are summarized in the Table given on pages 263–4.

The tumour is commonly of large size by the time it occasions symptoms, such as abdominal pain and swelling. Our largest specimen measures 25 × 17 × 15 centimetres, but even larger ones are described. It is usually unilateral, but may be bilateral, and is inconstantly associated with ascites, usually slight in amount.

The surface of the tumour is pale, usually lobulated and free from adhesions. In large tumours normal ovarian tissue cannot be distinguished, though in smaller ones (e.g., Case 3) a capsule

surrounds the growth, apparently derived from the ovary, and suggesting that the growth originates from the more central parts of the ovary.

The cut surface of the tumour is usually pinkish white and flecked with blood. The surface may be either granular or brain-like. When stained for fat the tissue usually gives only a feeble reaction. It is not always possible to distinguish the seminoma macroscopically from fibroma of the ovary. Many of the smaller tumours, if bilateral, to the naked eye resemble the Krukenberg tumour. The distinction from sarcoma is discussed later.

The only example of secondary growth in our series occurred in the opposite ovary (Case 6), and secondary growths on the peritoneum or distant metastases are usually absent, even when the tumour has attained a large size.

Microscopically, the tumour consists of masses of cells like spermatocytes, lying in spaces enclosed by a fine fibrous reticulum, which is continuous with coarser strands of supporting tissue (Figs. 1 and 2). These spaces in testicular seminomata are tubular, though according to Meyer the tumour originates outside the seminiferous tubules, invades them, and grows along them, but in ovarian seminomata a true tubular appearance is not seen, and the fibrous septa seem rather to divide the tumour into irregular clumps of cells or alveolar spaces. The cells lying in these clumps resemble spermatocytes on account of their large spherical nuclei, very frequently showing some phase of mitosis, though this is sometimes of a bizarre type (Fig. 3). The cytoplasm of these cells tends to be dissolved in paraffin sections, leaving a somewhat collapsed cell outline and vacuolated interior. This appearance is due to the somewhat lipoid nature of the cell contents. During mitosis the cell swells markedly.

In addition, another type of cell is almost constantly present, and appears to be of some importance in the microscopic diagnosis of seminoma. These cells resemble, and, in fact, probably are, lymphocytes, being small, round and darkly staining, with the nucleus almost filling the whole cell. They are arranged chiefly in strands along the fibrous septa in relation to the blood-vessels, the walls of which are well formed. Extensive areas of necrosis are sometimes present.

Giant-cells with nuclei arranged round their periphery, usually in a horse-shoe shape, are found in the stroma of some tumours. However, none of the cases in this series show giant-cells, but their appearance is strikingly shown in a section

from the collection of Dr. Walter Schiller, and reproduced with his kind permission (Fig. 4). According to the latter writer, these cells are concerned in the removal of lipoid material resulting from break-down of the tumour.[4]

The resemblance to the testicular seminoma is very striking. In ovarian seminomata the cells are more often irregularly arranged than in testicular tumours, though it is, in some cases, by no means easy to distinguish them by examination of a single section. The only tumour with which the seminoma is at all likely to be confused is the sarcoma of the ovary. Indeed, the writer has found cases microscopically similar to the seminoma, but with the tumour cells reduced in size and the characteristic lymphocytes absent, somewhat resembling a sarcoma. In this type of growth the Fallopian tube is commonly infiltrated, and death from metastasis is frequent. Indeed, the two types of growth seem sometimes to merge into a common anaplastic type.

My own conclusions about the seminoma ovarii are in agreement with those of Robert Meyer. (1) That the tumour frequently occurs in young patients, often in the second and third decades of life. It will be noted that one of our series occurred in a child of 4 years (Case 4). (2) That in some cases it is associated with imperfect sexual development, e.g. Case 1. The patient is, however, sometimes parous; indeed, a case has recently been described by Stabler and Grieg Thompson[5] of one of these tumours obstructing labour, and one of these tumours in our series was removed soon after delivery (Case 7). (3) That the tumour is not highly malignant. In the only case in which metastasis was known to have occurred in our series this was in the opposite ovary (Case 6). The Fallopian tube was not infiltrated in any of the cases.

Because of the remarkable resemblance of the ovarian to the testicular seminoma, it seems likely that the tumour originates from cell inclusions in the ovary, dating from the indifferent stage of development of the gonad. It will be recalled that in embryos up to 7 centimetres in length, i.e., approximately 7 weeks, it is impossible to say to which sex the gonad is to be assigned (Keith[6]). Should such indifferent cells persist in the ovary, which in extra-uterine life take on malignant characters, then a seminoma will arise. The cells seem, therefore, to have lost their power to develop into mature germinal tissue, but to have retained their property of tumour formation, and when this occurs their germinal (in this case testicular) nature is revealed. This degeneracy may or may not be shared by the

whole gonad. When it is (i.e., in cases of ovotestis), Schiller has postulated a "chromosomal malformation" of the gonad.[4] None of our cases was sufficiently recent to have had hormonal investigations carried out on them. It is generally stated that the tumour produces no internal secretion. However, in a case of testicular seminoma recently studied large quantities of prolan were excreted in the urine which disappeared on X-ray therapy. Further investigation is needed on this point. Its association with abnormal sexual development is characteristic, and cases have been described of a seminoma being found on one side, together with an ovotestis on the other.[7] (See case of Polano quoted by Meyer[3]).

It might be thought at first sight that this tumour in some way inhibited the development of secondary sex characters. A scrutiny of such a case as number 1 of our series makes it apparent that this cannot be so. In this case, the maldevelopment of the Müllerian system dates from early foetal life, while the tumour, which, as has been said, is rapidly growing, clearly was of recent origin. It is evident, therefore, that females in whom the genital organs are maldeveloped are, for some reason, prone to develop this tumour. This has been observed also to be true of males with imperfect sexual development, such as cryptorchism and pseudohermaphroditism.[8] It should be emphasized, however, that this imperfect development is present only in the minority of cases.

Recognition of the tumour is important, since the prognosis is relatively far better than in seminoma of the testis or of true ovarian sarcoma, with which the seminoma is often confused. This relatively favourable prognosis is improved by the fact that both the tumour and its metastases are highly sensitive to X-rays. It is evident from a survey of the reported cases of sarcoma of the ovary, such as that occurring in children, compiled by Gittins and Hawksley,[9] which includes the cases of Doran and Bland-Sutton, that the seminoma has formerly been frequently misinterpreted as a sarcoma.

From the standpoint of the surgeon, if a solid non-adherent ovarian tumour is found at laparotomy in a young patient, it alone should be removed and the likelihood of its being a seminoma should be borne in mind, and this diagnosis confirmed or excluded by microscopy later. If at operation the Fallopian tube is found to be infiltrated, the tumour, uterus and both appendages should be removed, since the growth is probably not a seminoma but a sarcoma or carcinoma, and deep X-ray

therapy given later. Ascites alone is an equivocal sign, since it is sometimes present in benign solid ovarian tumours such as the fibroma or fibromyoma, but if present in large quantities, or if blood-stained it is a sign for radical surgical and X-ray treatment.

If the diagnosis of seminoma is confirmed microscopically the question of deep X-ray therapy arises. Patients with these tumours are usually young and deep X-ray therapy would sterilize them by irradiation of the opposite ovary. This is, of course, specially undesirable in a patient otherwise normally developed sexually and in whom the opposite ovary was found to be normal at operation.

In the writer's opinion X-ray therapy should be withheld in cases in which signs of metastasis are not found at operation. A relatively good prognosis can then be given, but a careful follow-up of the patient should be made and X-ray treatment given if any fresh mass can be felt in the pelvis on bimanual examination or if there is any suggestion of ascites developing.

Deep X-ray therapy or teleradium should be reserved for the following types of cases only, viz. :—

(*a*) Any case in which there is the least suspicion of metastasis.

(*b*) When the patient is sexually neuter, or sexually imperfectly developed and, *ipso facto*, sterile.

(*c*) When it has been necessary to remove bilateral tumours.

In conclusion the writer must express his indebtedness to all the members of the obstetric staff, past and present, of the University College Hospital, whose material has been used in the preparation of this paper. Dr. Herbert Spencer's collection of gynaecological specimens, together with its catalogue, was especially valuable. To Professor G. R. Cameron, Professor F. J. Browne, and Mr. Clifford White I am particularly indebted for criticism and help. The microphotographs were taken for me by Dr. A. S. Aldis.

TABLE OF CASES.

Number	Age of patient	Clinical history	Tumour
1	31	No trace of vagina except urogenital sinus. Uterus absent. No pubic hair. Breasts rudimentary. Well 6 years after operation.	Unilateral, from left side, measuring 19 × 15 × 10 cm. Surface smooth and lobulated. On section, solid with very thin capsule, white granular and infiltrated with blood. Right ovary normal.
2	39	4 para. Complained of abdominal pain and swelling and irregularity of menstruation with menorrhagia. Well 8 months after operation.	Unilateral from left side, measuring 18 × 20 × 10 cm. Nodular surface. On section, solid, pinkish, with oedematous appearance. No true capsule visible. A little ascites present.
3	—	Unknown. Specimen sent from another hospital, as pathological diagnosis was uncertain.	Ovoid, measuring 8.5 × 5.0 cm. Surface smooth and slightly lobulated. Cut surface pale, brain-like, with thin capsule present.
4	4	Mother noticed lump in child's abdomen. No other symptoms.	Unilateral with long pedicle. Soft, solid homogeneous tumour.
5	24	Unknown. Well 2 years after operation.	Unilateral from right side, measuring 21 × 18 × 10 cm. Smooth lobulated surface. On section, solid with one small cystic space. Cut surface homogeneous but flecked with blood.
6	16	Menstruation began at 13 and was normal. Tumour said to have grown rapidly. Patient died of recurrence in opposite ovary.	Originated from left side, measuring 25 × 17 × 15 cm. Surface lobulated and smooth, except in a few places where growth penetrates surface. On section, pale, granular surface, centre of tumour necrotic and cystic. Similar tumour found post-mortem on right side.

Number	Age of patient	Clinical history	Tumour
7	24	2-para. Menstruation started at 13, was normal. Admitted to hospital because of bleeding 10 weeks after confinement.	Unilateral from left side, adherent to omentum and abdominal wall. Weight 4 lb. 15 oz. Surface lobulated. On section, solid with one small area of cystic degeneration and others of myxomatous appearance. When stained for fat showed only slight reaction. Right ovary normal.

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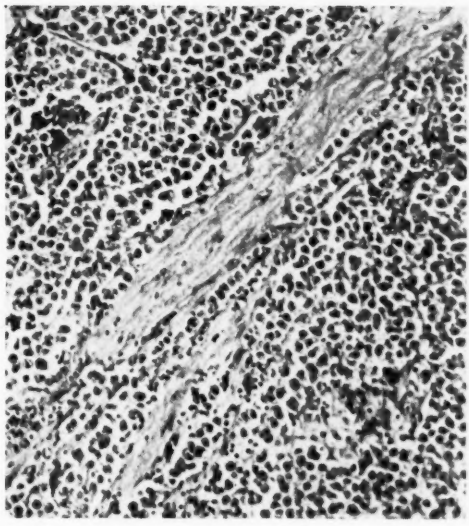

FIG. 1.
General appearance of tumour. Cells closely packed. Strands of supporting stroma seen. (×60).

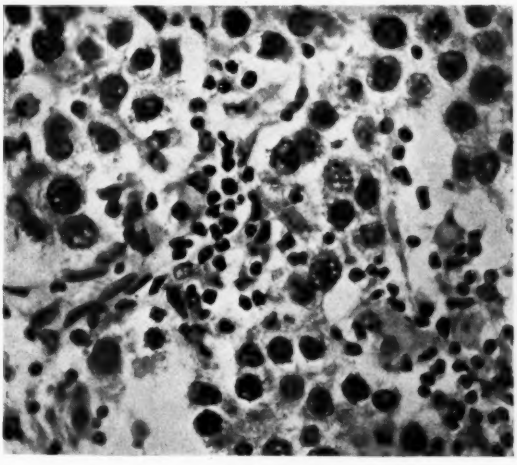

FIG. 2.
Showing the two essential types of cell, the larger spermatocyte-like cells and the smaller lymphocytes. (×480).

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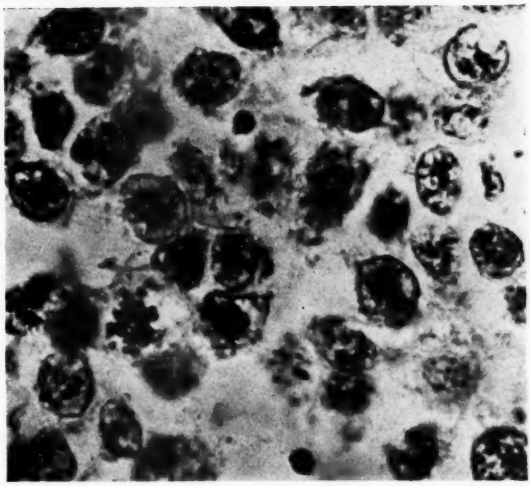

FIG. 3.
Spermatocyte-like cells. Two are undergoing mitosis. (×900).

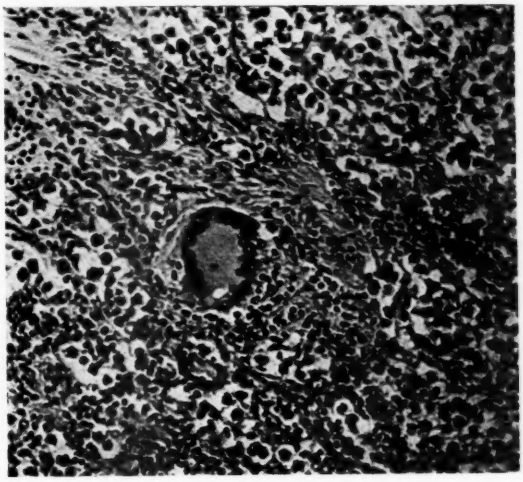

FIG. 4.
Giant-cell with horse-shoe nucleus. Stroma full of lymphocytes. Tumour cells more loosely arranged than in Fig. 1. (×68).

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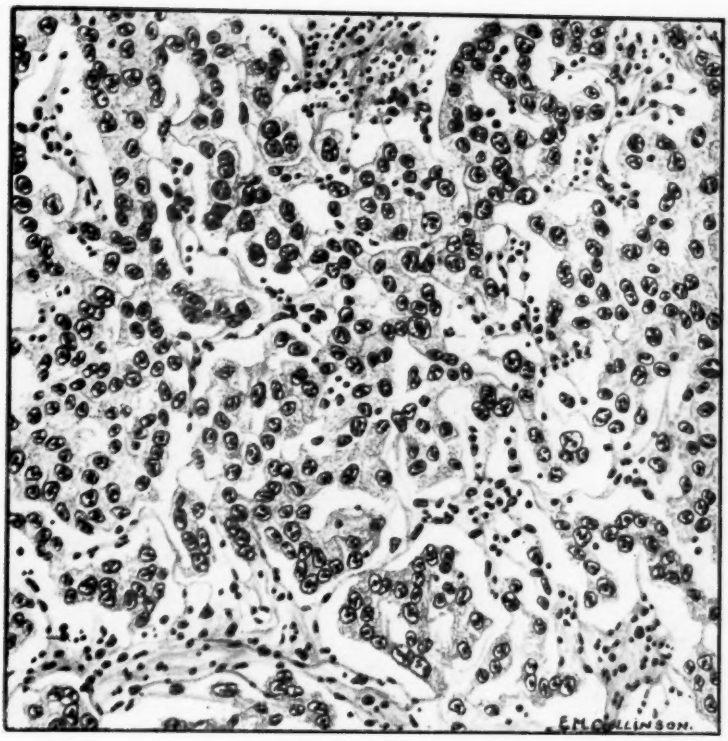

FIG. 5.

TYPICAL OVARIAN SEMINOMA.

The large size of the spermatocyte-like cells can be gauged from the lymphocytes with which the stroma is laden.

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Hydatidiform Mole: a Statistical and Clinical Study*

BY

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THE present study was undertaken with the idea of ascertaining particularly (1) the frequency of occurrence, (2) the effects of age and parity upon its production, and (3) duration of pregnancy, in Indian subjects. In order to find out whether there existed any racial effect, the results were compared with similar figures collected from world literature. The material for subject matter is derived from two sources, firstly from the published reports of different hospitals both in India and abroad, and, secondly, a detailed analysis of 42 cases of hydatidiform moles from Sir Kedarnath Maternity Hospital and Eden Hospital, two of the largest maternity hospitals in Calcutta.

INCIDENCE.

The incidence of hydatidiform mole has been variously estimated by different authors. In the majority of cases the figures have been arrived at from hospital records, while in others the source is not mentioned, and hence it is difficult to evaluate the importance of such figures. A glance at Table I will show how widely the figures vary from 1:204 to 1:20,000. The table has been arranged in numerical order.

The existence of hydatidiform mole is in far greater frequency than commonly supposed. Each decade has indicated an increase in frequency. In 1827, Madame Boivin[1] estimated it at 1:20,000. Slowly it rose to 1:10,000. The incidence is now estimated to be nearly 1:200 or 300 (Brooke Bland).[2] This figure is probably not a true indication of its occurrence, particularly in India, where a vast majority of patients are confined at home. Moreover,

* Read at the Twenty-fifth (Silver Jubilee) Session of the Indian Science Congress, held at Calcutta, January 1938.

at the exclusively maternity clinics comparatively few cases are seen, as such patients have a tendency to miscarry early and are more likely to go to the gynaecological clinics where they are treated as early abortions.

In the present series the frequency is worked out from a total of 222,542 cases (including full-time and premature labours, miscarriages and abortions), of which 108,951 are Indians and 106,063 Europeans. The rest of the cases are taken from the Maternity Bungalow, Hong Kong, where the majority of the patients are Chinese. The average frequency in Indian hospitals is 1:502; in England it is 1:835. The average frequency in all hospitals combined is 1:625 (Table II).

Aetiology.

The aetiology of this condition is still unknown. Many theories have been put forward from time to time to explain the occurrence of mole. The following have been enumerated as causes by different authors.

(1) Pre-existing endometritis (Virchow).[2a] (2) The presence of uterine fibroids. (3) Obliterating endarteritis of the vessels of the chorionic villi (Durante).[3] (4) Some grave maternal dyscrasia, e.g., syphilis, cancer. (5) Some obscure foetal disease (probably syphilis). (6) Foetal death. (7) Abnormal secretion of corpus luteum (Fraenkel).[4] (8) Effect of emmenagogues (Keiffer).[5] (9) Increased activity of the pituitary (Aschheim).[6]

Arguments in favour of each of the above have been put forward by its author. The actual exciting cause of the degeneration is still unknown—probably several exist. The presence of a diseased decidua in case of moles and the recurrence of the affection point to the endometrium as the cause. De Lee[7] thinks that probably endometritis will explain most cases as the nutritional condition of the placental site is vitally important to the health of the ovum.

Recent writers consider endometrial change as secondary and seek the initial factor in the ovum itself. In support of the latter theory rare instances of twin pregnancy in which one ovum may be normal, while the other presents the characteristic lesion, are often quoted.

Age. It is essentially a disease of the child-bearing period. According to most authors, the disease originates during the latter part of the reproductive period. Sunde, quoted by Williams,[8] says it occurs two and a half times more frequently after the

fortieth year if the total number of pregnancies is considered. Recent statistics, however, show that age of the women has very little influence on its production. It may occur at any age, at any pregnancy.

The age of the youngest patient noted in the literature is 9 years (Molitor[9]) and the age of the oldest is 55 years (Feenders).[10] According to Brooke Bland 70 per cent of cases occur between the ages of 20 and 35, and 30 per cent either before or after this period.

In our series it would appear from Table III that among Indians the greatest number of cases occurred between the years 21 to 30, with nearly equal number of cases below 20 and above 31 years, whereas among Europeans the greatest number of cases also occurred between 21 and 30 years followed by fourth, fifth and second decades in order of frequency. The difference is rather significant. In both cases the peak is reached in the third decade, but in Indians there is a more or less equal fall on either side, whereas in Europeans the fall is gradual. It will also be seen that in Indians the greater number of cases (67.5 per cent) occurs below the age of 30 years, while in Europeans the greater number of cases (56 per cent) occurs after the age of 30 years. The incidence of average age as per Table IV is 27.3 years in Indians and 28.5 years among Europeans.

The occurrence of a greater number of cases at an earlier age and evidence of an earlier incidence of average age among Indians can only be explained on grounds of early marriage and motherhood.

Parity. Though hydatidiform mole occurs with much greater frequency in multiparae, it is not so rare in primigravidae as was formerly thought. From Table V it would appear that 70 to 90 per cent of cases occur in multiparae. In our series multiparae contributed 88 per cent of cases. But if individual parity is considered hydatidiform mole occurs with much greater frequency in primigravidae, varying from 10 to 18 per cent. It will be evident from Table VI that the greatest number of cases occurred in patients who had only one child. Next to primiparae most cases occur in primigravidae and in women with two children. It becomes progressively less after the tenth pregnancy.

If any deduction is to be drawn from the above figures it must be that most cases occur in the first three pregnancies.

It is often stated that rapid and recurring child-bearing favours the growth of hydatidiform mole. We have not been able to corroborate the truth of such a statement from our series.

Pathological Anatomy.

It is now generally believed that there are two forms of hydatidiform mole, one of which is, and the other is not, followed by the development of chorion epithelioma. In one we find mainly the hydropic change with little or no proliferation of the epithelium, while the other shows sheets of rapidly growing syncytium and Langhans's cells with only moderate cystic degeneration. Between these two types there are many specimens showing varying degrees of both types of changes. Accordingly, moles showing mainly cystic change with little epithelial proliferation as an outstanding feature are much more apt to exhibit invasive characteristics, penetrating the uterine wall, causing metastasis and finally forming true chorion epithelioma.

The decidua in a case of vesicular mole is usually abnormally thick, and shows considerable round-celled infiltration on microscopic examination. This is regarded by some as a defensive change which enables the decidua to offer greater resistance to the eroding action of chorionic epithelium and thus to protect the uterine wall against excessive penetration.

In about 50 per cent of cases hydatidiform mole is accompanied by bilateral, multilocular, luteal cysts, of varying size, containing a thin, clear or watery straw-coloured fluid, and lined by two or three layers of lutein cells. The association of lutein cystoma with hydatidiform mole has given rise to much speculation. Certain authors hold that they stand in some aetiological relation to the mole; others hold that they are secondary to it; while a third group think that the process merely represents an exaggeration of the theca luteal cell proliferation which is found in normal pregnancy.

The fact that certain percentages of cases are accompanied by lutein cystoma is strongly against the view that such cystomata play an aetiological role. On the other hand, that such tumours undergo spontaneous regression within a few months after the expulsion of the mole indicates that there must be some genetic relation between the two processes. Probability is lent to the view that these cysts develop as the result of excessive amount of anterior pituitary-like hormone secreted by the mole.

Clinical Features.

Signs of toxaemia of pregnancy, particularly hyperemesis, albuminuria, hypertension and oedema of the lower extremities are of frequent occurrence. Brews[11] found albuminuria in 35

per cent of his cases. On rare occasions eclampsia has been known to supervene. Nephritis has often been found in association with these moles.

The usual finding in the majority of cases is that the fundus of the uterus lies at the level of the umbilicus after 3 months' amenorrhoea. It will be apparent from Table VII that the figures of Briggs, Brews and Mathieu differ so widely that a definite conclusion cannot be reached regarding the percentage of different sizes of the uterus. It is generally believed that expulsion of the moles usually occurs spontaneously at about the end of the fourth month, but it may occur earlier or as late as the seventh month.

In the present series the period of amenorrhoea before the birth of the moles was mentioned in 35 patients. As in Table VIII the period of amenorrhoea has been noted in months calculated from the last menstrual period. In 29 patients, i.e., in 82 per cent of cases, the duration of amenorrhoea was 3 to 5 months. In one case there was amenorrhoea for 1 month and in another for 7 months.

Diagnosis.

The early diagnosis of hydatidiform mole is often difficult. The vaginal bleeding is usually the first symptom that pregnancy is abnormal. Rapid enlargement of the uterus, absence of the foetal parts and foetal movements on palpation, the doughy consistence of the uterus and general evidences of illness arouse a suspicion of a vesicular mole. If with these the vaginal bleeding contains typical vesicles the diagnosis becomes certain.

Now and again cases occur in which typical signs and symptoms are absent, and it is in these cases that the diagnosis is difficult. Since the condition may give rise to severe toxaemia with a fatal result, or become malignant before it is expelled from the uterus, once a suspicion of vesicular mole arises in the mind, one should not remain satisfied until and unless it is proved otherwise. In case of difficulty one has to take recourse to other diagnostic methods, particularly the Aschheim-Zondek test or one of its modifications, and X-ray.

The Aschheim-Zondek reaction is much more intense than during normal pregnancy. On the other hand, a normal pregnancy reaction does not exclude the possibility of a mole. A negative reaction which does not agree with the clinical picture might be false. The greatest pitfall in the test is the false nega-

tive. It should be remembered in this connexion that normally the laboratory error is up to 2 per cent.

It is difficult to diagnose pregnancy by X-ray films, due, among other things, to the relatively slight density of the foetal skeleton. According to Calloway,[12] quoted by Whitridge Williams, an X-ray diagnosis of pregnancy can be made in only one-third of the patients at the fifth month and in half at the sixth month. A negative X-ray film will not be of much assistance before the third month, whereas after this, if repeated X-ray examinations taken at different positions fail to show a foetal shadow, a diagnosis of vesicular mole is warranted, provided other clinical symptoms are present.

Bortini[13] advised hysterography by injecting a contrast medium only after repeated failure of X-ray to show foetal bones. He thinks that the X-ray picture is so characteristic for a hydatidiform mole that it cannot be mistaken for other conditions. Obviously such a procedure is rather drastic and is not only unnecessary but should be condemned. In the vast majority of cases a diagnosis can be made by clinical symptoms only if one remembers its possibility.

Prognosis.

The degree of malignancy and the amount of invasion cannot be accurately determined by microscopic examination of the expelled mole. The foetal cells left behind in the endometrium, or in the uterine musculature, may or may not proceed to the formation of chorion epithelioma. Hence, the prognosis is uncertain.

According to Schumann[14] the mortality in patients suffering from vesicular mole is higher (15 to 20 per cent) than that following any obstetrical complication except puerperal sepsis and premature separation of placenta. Most authors, however, place it at 10 to 12 per cent, as will be seen from Table IX.

In our series the mortality is comparatively low, being 7 per cent.

The incidence of chorion epithelioma following hydatidiform mole is not accurately known. It varies rather widely, ranging from 1 to 44 per cent (Table X). Mathieu[15] reports that in his series practically 80 per cent of chorion epitheliomata were found within 20 days after passage of the mole. Chorion epithelioma arising from hydatidiform mole displays less malignancy than when it follows normal pregnancy.

In rare instances at varying periods after expulsion of the mole, small purplish or reddish tumours may appear in the vagina or vulva. On microscopic examination these are found to consist for the most part of blood, through which are scattered oedematous villi showing characteristic changes. The uterus in these cases is normal in size. Recent observations show that they are due to accidental transportation of particles of benign growth.

The birth of one or more moles does not preclude the possibility of future normal pregnancies, as a vesicular mole has not any effect on subsequent fertility. A hydatidiform mole has been known to recur in subsequent pregnancies.

Treatment.

As soon as the positive diagnosis is made the uterus should be immediately emptied *per vaginam*. The dangers of the operation should be borne in mind, particularly perforation and haemorrhage. Perforation may easily occur either by finger or by curette, if one is used.

Other treatments advocated are vaginal or abdominal hysterotomy and abdominal hysterectomy. Abdominal hysterotomy, first advocated by Schumann, "in view of the danger inherent to this abnormality," is not favoured by most authors. But abdominal hysterectomy has certainly a place in the treatment of vesicular mole, especially in women nearing the menopause and with the cervix closed. For in such a patient not only are the chances of chorion epithelioma higher but there is also no great need for conserving the uterus. It is interesting to note in this connexion that Mathieu, in an analysis of 127 cases of vesicular moles, found that hysterectomy *per se*, as treatment of the mole, would not have saved any lives. According to Essen-Möller[16] about 50 per cent of molar pregnancies end spontaneously.

In the present series manual evacuation from below was performed in 78 per cent of cases; nearly 5 per cent of cases ended spontaneously; and in 1 case, or in 2.4 per cent, hysterectomy was performed (Table XI).

Conclusions.

The frequency of vesicular mole among Indians is 1:502; among Europeans 1:835; in Europeans and Indians combined the average frequency is 1:625.

The largest number of cases among Indians occurred between the years 20 and 31, and 65 per cent of all the cases taken occurred below the age of 30.

The average age of incidence among Indians was 27.3 years as against 28.9 years among Europeans.

Among Indians 88 per cent of cases occurred in multiparae. If individual parity is considered the greatest number of cases, 21.4 per cent, occurred in patients who had only one child.

The duration of pregnancy before the birth of the moles in 82 per cent of Indian patients was 3 to 5 months.

Most of the patients, 78.4 per cent, were treated by manual removal of the mole from below. In about 5 per cent of cases the moles were spontaneously expelled.

The mortality in our series of Indian patients is 7 per cent.

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TABLE I.

Authors' statistics.

Velasco	1:204	Lwoff	1:1,500
Gordon	1:214	Jellet and Madill ...	1:1,551:7
Grenn-Armytage and Dutta	1:230	Dubisay and Jennin	1:2,000
Kroemer	1:250	Bustamante	1:2,000
Dongen	1:250	Brodhead and Kassebohm	1:2,000
Cortiguera	1:257	Remmelt	1:2,000
Meyer, A. W. ...	1:261	Scharman	1:2,334
Mayer, K.	1:310	Williamson	1:2,400
Essen-Möller	1:333	Cameron	1:2,500
Seitz	1:500	Shlenker	1:2,500
Hirst	1:535	Craigin	1:3,000
Kronig	1:728	Edgar	1:3,750
Das, K.	1:790	Donskoj	1:4,058
Engle	1:800	Mann	1:8,000
Korn	1:1,250	Boivin	1:20,000

TABLE II.

Hospital statistics.

GREAT BRITAIN.

Hospitals	Number of moles	Number of pregnancies	Ratio	Date
Queen Charlotte's Hospital ...	3	19,558	1:6,519	1923–32
Hospital for Women and Children, Leeds	17	1,863	1:109.5	1916–31
Edinburgh Royal Maternity and Simpson Memorial Hospital	38	18,230	1:479.7	1923–32
Maternity Department, St. Mary's Hospital, Manchester	39	15,764	1:404.2	1921–31
Liverpool Maternity and Ladies Hospital	1	12,287	1:12,287	1920–25
The Princess Mary Maternity Hospital, Newcastle-upon-Tyne	5	8,538	1:1,707.6	1932–34
Rotunda Hospital	24	29,832	1:1,242.6	1922–30
Total	127	106,063	1:835	

INDIA.

Carmichael Medical College, Calcutta	21	4,755	1:226.4	1922–32
Chittaranjan Seva Sadan, Calcutta	61	11,501	1:188.5	1926–35
Baldeodas Maternity Hospital, Calcutta	20	9,632	1:481.6	1927–33
Government Lying-in Hospital, Madras	96	78,878	1:821.6	1881–1933
Victoria Hospital for Caste and Gosha, Madras ...	19	4,185	1:220.3	1908–12
Total	217	108,951	1:502	

HONG KONG.

Maternity Bungalow	12	7,528	1:627.3	1930–34
Grand total	356	222,542	1:625.1	

TABLE III.

Age incidence.

Author	Number of cases					Percentage					Summary	
	Under 20	21–30	31–40	41–50	Above 50	Under 20	21–30	31–40	41–50	Above 50	Total No.	Per-centage
Bloch	—	15	20	14	—	—	30.6	40.8	28.6	—	49	100
Brodhead and Kassebohm	—	6	3	1	—	—	60	30	10	—	10	100
Donskoj	—	8	2	—	—	—	80	20	—	—	10	100
Fricker	—	18	15	8	1	—	42.9	35.7	19	2.4	42	100
Häberlein	—	19	22	18	2	—	31.1	36	29.5	3.4	61	100
Hiernack	5	33	35	19	4	5.2	34.4	36.4	19.8	4.2	96	100
Imhoff	14	112	94	52	8	5	40	33.6	18.6	2.8	280	100
Kehrer	2	19	18	9	2	4	38	36	18	4	50	100
Kroemer	—	10	6	—	1	—	59	35.2	—	5.8	17	100
Metzges	5	34	37	18	2	5.2	35.4	38.5	18.8	2.1	96	100
Oster	1	7	8	4	—	5	35	40	20	—	20	100
Thürigen	5	28	8	9	—	10	56	16	18	—	50	100
Williamson	2	10	7	5	1	8	40	28	20	4	25	100
Total (Europeans) ...	34	319	275	157	21	4.2	40	34	19.4	2.6	806	100
Das (author) (Indians)	9	18	9	4	—	22.5	45	22.5	10	—	40	100
Grand total	43	337	284	161	21	5	40	33.5	19	2.5	846	100

TABLE IV.

Average age of incidence in years. (After Brodhead and Kassebohm.)

Author	Average age	Number of cases
Brodhead and Kassebohm ...	30.4	10 Europeans
Poten	32	6 ,,
Donskoj	25	10 ,,
Briggs	28	23 ,,
Gromazki	29.6	6 ,,
Robertson	28.4	8 ,,
Weighted average	28.5	63 ,,
Das (author)	27.3	40 Indians
Weighted average	28	103 Combined

TABLE V.

Parity.

Author	Percentage	
	Primigravidae	Multiparae
Brodhead and Kassebohm ...	30	70
Kehrer	10	90
Schweizer	18	82
Hirst	29	71
Brooke Bland	30	70
Mathieu	37	63
Brews	26	74
Donskoj	30	70
Thürigen	18	82
Williamson	12	88
Das (author)	12	88

TABLE VI.

Parity.

	Thürigen	Kehrer	Combined statistics	Donskoj	Williamson	Das (author)	Total	Thürigen	Kehrer	Combined statistics	Donskoj	Williamson	Das (author)
Parity	Number							Percentage					
0	—	—	14	3	3	5	25	18	10	16.2	30	12	11.9
1	—	—	5	4	7	9	25	12	12	5.7	40	28	21.4
2	—	—	9	1	4	6	20	8	8	10.3	10	16	14.3
3	—	—	12	—	—	4	16	6	16	13.8	—	—	9.5
4	—	—	8	1	3	6	18	10	10	9.2	10	12	14.3
5	—	—	7	—	1	3	11	6	6	8	—	4	7.1
6	—	—	5	—	—	3	8	6	4	5.7	—	—	7.1
7	—	—	10	—	—	—	10	8	16	11.6	—	—	—
8	—	—	5	—	2	2	9	4	6	5.6	—	8	4.8
Above 8	—	—	12	1	5	4	22	12	12	13.8	10	20	9.6
Total	—	—	87	10	25	42	164	100	100	100	100	100	100

TABLE VII.

Size of the uterus.

Author	Percentage		
	Bigger	Same	Smaller
Briggs	19	5	76
Brews	64.8	13.6	21.6
Mathieu	49	36	15

TABLE VIII.

Duration of pregnancy before birth of moles.

Month	Number of cases (Indians)
1	1
2	1
3	9
4	10
5	10
6	3
7	1

TABLE IX.

Mortality.

Author	Percentage
Brews	1.4
De Lee	16
Dorland	10
Williamson	20
Findlay	10.5
Gordon	9
Mathieu	2.36
Sande	5
Das (author)	7 (Indians)

TABLE X.

Incidence of chorion epithelioma following mole.

Author	Percentage
Brews	8.3
Findlay	31.4
Fränkl	7½–33
Senarcleus	13
Pallosan and Violet ...	44
Novak	1

TABLE XI.

Treatment.

Uterus evacuated with digital separation and removal with ovum forceps	33 or 78.4 per cent
Spontaneous expulsion	2 or 4.8 ,,
Surgical induction of abortion of mole with cervico-vaginal pack	6 or 14.4 ,,
Hysterectomy	1 or 2.4 ,,

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The Diagnosis of Intra-Uterine Death by a Spectrographic Method

BY

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THE object of the present note is to record a spectrographic method of diagnosing intra-uterine death of the foetus. It arose from a study of the amounts of different oestrogenic substances in the urine of pregnancy and is based upon a specific spectroscopic change that can be demonstrated in the urine of women carrying a dead foetus, this change coinciding with actual or impending intra-uterine death.

ABSORPTION SPECTROSCOPY.

Absorption spectroscopy depends upon the ability of many solutions to absorb light. With some solutions the absorption of light is greatest at a certain specific wave-length in the spectrum, when the absorption is said to be selective, but the degree of absorption is always directly proportional to the thickness, or depth, of the solution, and to its concentration. Hence the concentration of such solutions can be calculated by simple proportion if the absorption of the pure product is known.

THE OESTROGENIC SUBSTANCES.

Pregnancy urine contains oestrone, a hydroxy-ketone, and oestriol, a trihydric alcohol, both oestrogenic substances occurring partly free and partly in a combined form. The free oestrin can be extracted from fresh untreated urine with ether, while the combined form of oestrin can only be extracted with ether after preliminary acid hydrolysis of the urine. Acid hydrolysis converts the whole of the oestrogenic material into the uncombined state, when it is readily extracted by means of ether. A simple technique (Procedure I) thus yields an extract containing all the oestrone and oestriol, but contaminated with other substances, while a more lengthy technique (Procedure II) permits the elimination of such contaminants.

In an attempt to find suitable extracts for spectrographic study both procedures were employed in these experiments.

Procedure I.

A 200 to 300 c.c. sample of urine of pregnancy, adjusted to *p*H 1 to 2 with concentrated hydrochloric acid, is refluxed at 100°C. for 3 hours on a water bath. On completion of the hydrolysis of oestrogenic complexes, the cold solution is extracted 3 times with 100 c.c. of freshly re-distilled ether. The etherial extract is washed with bicarbonate of soda and water, the solvent removed and replaced by 5 c.c. of spectrographic alcohol (specially purified ethyl alcohol) and its ultra-violet absorption determined, using a 1 to 5 mm. cell.

Procedure II.

The crude etherial extract obtained as in Procedure I is subjected to further treatment on the lines laid down by Cohen and Marrian[1] for the separation of oestrone and oestriol. Their separation is based on the fact that oestriol may be readily extracted from an etherial solution with dilute aqueous alkali hydroxides, while *N* sodium hydroxide effects a complete extraction of oestrone from toluene. In the present series oestrone and oestriol were not separated, but the entire extract was freed from ether, dissolved in toluene and re-extracted with *N* sodium hydroxide. After acidifying with hydrochloric acid the product was again extracted with ether and examined as in the final stages of Procedure I.

Absorption Spectroscopy of the Oestrogenic Substances.

Pure oestrin (B.D.H. crystalline oestriol) was found to exhibit selective absorption, with a broad band having its maximal absorption in the ultra-violet near 281mμ, and a minimal about 260mμ. Both oestrone and oestriol have almost identical absorption curves. Accordingly, the absorption intensity of all the oestrogenic extracts was measured at 281mμ.

Extracts from urine of normal and abnormal pregnancy were obtained employing the two techniques mentioned above and all were found to display a characteristic absorption band in the same region as that of pure oestrin. From the absorption intensity of these extracts the total oestrin (so-called) content of of the urines examined was estimated. In general it was found that the absorption intensity of extracts obtained by Procedure II was very nearly half that of extracts obtained by Procedure I

from similar urines, while in certain cases it was noticed that the absorption intensity of the two extracts was of the same order.

Further investigation was carried out in order to determine the significance of this phenomenon and the results which have emerged suggest that this striking difference is associated with intra-uterine death of the foetus.

Tables I and II record the results obtained from the spectrographic examination of the urine of a number of cases of intra-uterine death and a series of patients carrying a living foetus

TABLE I. PROCEDURE I.

Absorption intensity at 281mμ.

Normal cases (average of three estimations)	Intra-uterine death cases
13.0	7·7
12.6	7.0
20.5	5·9
12.0	10.4
14.0	5.0
18.0	—
17.0	—
18.0	—
14.0	—
Average: 15.5	Average: 7.2

TABLE II. PROCEDURE II.

Absorption intensity at 281mμ.*

Normal cases	Intra-uterine death cases
8.7	10.6
10.1	9·53
10.2	10.8
10.1	9·3
10.3	9.6
7·4	7·5
10.0	6.6
Average: 9.5	Average: 9.1

* If the absorption were due wholly to oestrin these figures would represent milligrams per cent. As the extract is contaminated, the scale is to that extent arbitrary.

It is clear from Table I that by using the simple technique (Procedure I) the selective absorption shown by extracts from the urines of patients in whom the foetus had died *in utero* is much less than that shown by similar extracts from normal pregnancy urines.

In contrast, it will be seen from Table II that the comparable figures from similar cases obtained by the second technique (Procedure II) are of much the same order for both the normal urines and the urines from women carrying a dead foetus.

These tables show that it is possible to diagnose intra-uterine death of the foetus by submitting the urinary extracts obtained by both preparative techniques to spectrographic analysis. If the foetus is alive there will be an appreciable difference between the two estimations, whereas if the foetus is dead the two estimations will be approximately the same. It is fully recognized, however, that in a matter of this kind caution must be shown in generalizing from limited data.

Among a number of urines examined spectrographically those from 12 patients (Table III) showed an absorption intensity considered to be characteristic of intra-uterine death of the foetus, and in each case the patient was subsequently delivered of a macerated foetus.

TABLE III.

Absorption intensity at 281$m\mu$.

	Procedure I	Procedure II
Mrs. H.	10.6	9.3
Mrs. M.	11.6	10.6
Mrs. S.	10.5	9.5
Mrs. S.	12.0	10.8
Mrs. S.	9.0	7.5
Mrs. R.	11.0	9.6
Mrs. G.	9.0	6.6
Mrs. J.	10.0	6.0
Mrs. McG.	9.3	10.0
Mrs. B.	11.0	10.0
Mrs. B.	17.0	15.0
Mrs. W.	16.0	18.0

(The figures in these columns are approximately the same, indicating intra-uterine death of the foetus.)

In four other patients in whom intra-uterine death of the foetus was suspected (Table IV) the spectrographic examination

of the urine suggested that the foetus was alive and the accuracy of this result was subsequently confirmed as each pregnancy proceeded normally.

TABLE IV.

Absorption intensity at 281mμ.

	Procedure I*	Procedure II
Mrs. F.	31.3	16.4
Mrs. D.	21.0	9.0
Mrs. H.	23.3	18.0
Mrs. L.	26.4	10.0

(The columns differ widely, indicating normality.)

* The higher figures recorded in this Table as compared with Table I are due to the fact that the urines were boiled for a longer time. Nevertheless, it will be observed that the relative difference between the two columns persists.

So far, only evidence in favour of this empirical test has been given, but in 3 cases (Table V) of suspected intra-uterine death of the foetus the results were misleading.

TABLE V.

	Absorption intensity at 281mμ.			
	Procedure I	Procedure II	Inference	History
Toxaemic cases:				
Mrs. H. ...	23.0	14.0	Foetus alive	Macerated foetus delivered
Mrs. C. ...	21.0	10.6	Foetus alive	Macerated foetus delivered
Anencephalic case:				
Mrs. McM. ...	17.0	18.0	Foetus dead	Foetus breathed

It will be seen that two of these patients were suffering from toxaemia, while the third carried an anencephalic foetus. It is to be expected that the hormone balance must be influenced by foetal abnormalities, in which well-known endocrine deficiency occurs, while in renal cases the excretory power is at fault. In either event the hormone content of the urine will be affected to an extent which may interfere with the test and, therefore, special caution must be exercised when applying this test to such patients.

Discussion.

Although it is at present impossible to explain this striking spectrographic phenomenon it is clear that the technique has a positive empirical value, and it is a legitimate inference from the results recorded in this paper that a substance absorbing in the same region as oestrin is absent, or greatly reduced in quantity, in the urine of women carrying a dead foetus.

We are thus led to postulate the existence of a hitherto unrecognized hormone in the urine of a normal pregnancy, with apparently a very definite role in normal gestation. Such a hypothesis implies that intra-uterine death of the foetus may be connected sometimes at least with a specific hormone deficiency or imbalance. This hormone imbalance may, of course, be either a cause of, or a sequel to, intra-uterine death.

An attempt was made to isolate this unknown product, and ultimately it was traced to the toluene residues of the Marrian technique. From 20 litres of urine, treated in small batches, a few milligrams of the final product were obtained in a crystalline form. This *x* product showed selective absorption near 294mμ, and had a melting point in the region of 225 to 230°C., while its biological reaction was oestrogenic.

However, until further information is available its identification is merely speculative, but from the facts obtained it is desirable that this problem should be further explored, and it is hoped that further research will establish the identity of the *x* product and elucidate its relation to the living foetus.

Summary.

1. An empirical spectographic test for foetal intra-uterine death is described.

2. The presence of an unrecognized hormone in the urine of pregnancy is suggested.

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Height of the Anterior Shoulder and its Relation to the Position of the Foetal Heart

BY

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IT has been proved that the recognition of the anterior shoulder is of great value, along with other signs, in arriving at the proper diagnosis in a case of pregnancy in the later months. By locating the shoulder, the exact position in a vertex presentation can be distinguished. By measuring the height of the shoulder from the top of the symphysis pubis, the engagement of the head in the pelvis can be determined almost to a certainty. By noticing the distance of the shoulder from the middle line, not only can the anterior position be differentiated from the posterior but the gradual approach of the anterior shoulder to the central line in the course of labour as it is being followed indicates that internal rotation is taking place. Further, when a patient is treated by a trial labour, following of the anterior shoulder enables one to judge of the progress of labour. The height of the shoulder is a sure guide to estimate the exact situation of the head in the pelvis when it is proposed to apply the forceps in a case of protracted labour, for the large caput succedaneum then formed is liable to mislead and give a false impression that the head is very low. Moreover, the height of the shoulder is also of service in denoting the exact site where the foetal heart-sounds should be auscultated. This is not stationary but varies according to the height of the anterior shoulder.

To determine the site of the foetal heart-sounds two lines can be drawn on the abdomen, one central and the other lateral. The central or middle line may be drawn between the umbilicus and the mid-point on the top of the symphysis pubis. The lateral line is drawn parallel to it and at some distance, the distance varying in the anterior and posterior positions.

In any anterior position, either the left or the right, the heart-sounds are heard on the lateral line, 2 inches away from the middle line. For measuring the height at which level the heart-sounds are heard best on the lateral line, it is convenient to make use of the central line. When the anterior shoulder is at the height of 2 inches, as is observed when the head is engaged and has reached the level of the ischial spines, the heart-sounds are heard on the lateral line at the level of 4 inches above the pubis as measured on the middle line. When the height of the shoulder is 3 inches, as it is seen when the head is half engaged and lying in the mid-plane of the pelvic cavity, the height is 6 inches above the symphysis, and at that level the heart should be listened to on the lateral line. When the height of the anterior shoulder is 4 inches, which indicates that the head is engaging, the level of the sounds is about 7 inches. When the head is floating the heart-sounds are heard at the level of the umbilicus and 2 inches away from it.

For listening to the heart-sounds in the posterior positions the lateral line is to be imagined from between $3\frac{1}{2}$ to 4 inches from the middle line, variations in distance being due to the exact position of the back.

From what has been said above it is advisable first to discover the height of the anterior shoulder and thus the amount of engagement of the head, and then it is easy to determine where the foetal heart should be auscultated. In this way one can readily find the exact site and not waste time in listening elsewhere. For instance, when the head is floating and the anterior shoulder is at the height of 5 inches, the heart-sounds cannot be heard anywhere except at the level of the umbilicus on the side of the back.

Wet-Specimen Demonstration Frames for Teaching Purposes

BY

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THE teaching of gynaecology, more than that of any other branch of medicine, is assisted by the demonstration of wet specimens. Particularly is that so on account of the fact that gynaecology as a subject is so dependent upon a thorough understanding of the pathological lesions involved and that the frequency with which part (or all) of the pelvic organs is removed provides a variety of pathological states to be appreciated. In fact one might say that a systematic and thorough presentation to the students of the various pathological conditions of the female pelvic organs, as relatively fresh specimens, is essential to their complete understanding of these conditions. The lantern slide, though helpful, does not induce mental receptivity on the part of the average student, and is too easily forgotten. There is a tendency for the student to look at lantern slides without seeing them, as it were. The potted specimen evokes the response that most students have to this type of demonstration—a relatively inaccessible specimen of abnormal colour and size which fails to impress.

The wet specimen, however, which can be demonstrated in the fresh state—while it still maintains its normal colour, size and appearance—and the salient features of which can be appreciated in their entirety by all the students of a large class is, to my mind, an invaluable aid to the instillation of the facts of gynaecological pathology into the minds of students.

To this end I have evolved the wet-specimen demonstration frames here shown. They consist of ordinary drawing-boards of various sizes slung from metal frames. The specimen is pinned to the board and the salient features of it can be written down in chalk thereon. A partial specimen, such as a tubal pregnancy or ovarian cyst, can be graphically indicated by drawing in the uterus or associated pelvic organs. A large specimen, e.g. fibroids

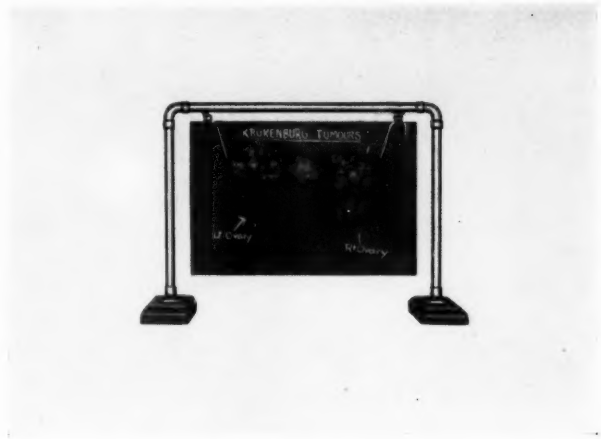
or cysts, can be slung by hooks in the frame itself with the board suspended behind the frame as a background. A list of facts such as differential diagnosis, or clinical signs or symptoms, can be written at the side. The impression gained by the student, therefore, is a composite one and is likely to be more easily retained.

These boards, moreover, have the advantage of demonstrating in this respect to *all* the students of a large class. The details and writing can be easily seen from the back of the class if the boards are flood-lit from the front of the lecture desk. For this purpose, say, 3 tubular electric lights can be fitted. A number of fresh specimens can easily be obtained by the lecturer from operations performed by him during the few days prior to the lecture and retained in their normal appearance in saline.

By the use of this simple apparatus, therefore, I feel that a part of our teaching which previously has seemed to me to be of direct interest to only a few of the bolder and more enthusiastic students—who would make a point of staying behind after the lecture to investigate specimens presented on trays, somewhat distorted and lacking in attraction—is now presentable to the whole class in a more interesting and easily assimilable form

WET-SPECIMEN BOARDS ON LECTURE DESK IN LECTURE THEATRE.

UNIV. OF MICH.



WET-SPECIMEN BOARDS.

WET-SPECIMEN BOARD.

The Cycle of the Woman.

BY

JULES SAMUELS, M.D., Amsterdam.

BY studying Fig. 1, designed by me, one will soon become acquainted with the hormonal influences which play a part in the cycle of the woman. The design gives a survey of all processes. It shows the relation of the cyclogram to the hypophysis, to ovulation, and to the endometrium.

In this connexion a new feature has been determined, namely, that there are two or more ova per cycle and not one as has always been presumed by scientists. In this connexion the question arises, why, despite innumerable operations, pathological, anatomical and post-mortem examinations, only one ovulation has been observed.

On studying the relevant literature it will be seen that some writers have found that ovulation takes place in the first half of the cycle and others in the second half. Ruge,[1] for instance, puts the period of ovulation at 8 to 14 days after the commencement of the last menstruation. After witnessing numerous operations Fränkel[2] decided that ovulation takes place between the eighteenth and the nineteenth day. Robert Meyer[3] was at first of the opinion that ovulation occurs on the eighth to the fourteenth day of the cycle. Later on he gave the eighteenth as the day of ovulation. Schröder,[4] who checked the results arrived at by Robert Meyer and Ruge, came to the conclusion that ovulation takes place between the fourteenth and the sixteenth day of the cycle. Halban and Köhler[5] put it at the eighth to eighteenth day, Shaw[6] the thirteenth to seventeenth, Müller[7] the twentieth, Allen[8] the twelfth to fourteenth, Grosser,[9] Fränkel and Triepel[10] the eighteenth to nineteenth day of the cycle, Knaus[11] 15 days, and Ogino[12] 12 to 16 days before the next menstruation. Why did these scientists arrive at such different conclusions? There is only one answer to such a question: they erroneously presumed that there is only one ovulation in each cycle. As, however, 2 ova are liberated in a cycle (and in the case of young girls even 3), as I can certainly demonstrate with the spectroscope, it must be that some of the scientists observed the first ovulation and some the second.

If only one ovum were liberated per cycle it would not be possible to bring the observations of an ovulation in the first and in the second part of the cycle into accord with the generally accepted presumption that there is a fixed period between ovulation and menstruation, or, in other words, that the corpus luteum has a specific term of life. The first scientists who ventured to attack the one-ovum theory were Fränkel and Grosser, who frequently assumed there was a second so-called violent, provoked or artificial ovulation in addition to the one ovulation. Robert Meyer, however, accounted for this by asserting that Fränkel had misjudged the age of the first corpus luteum and that he must have been dealing with a corpus luteum of the previous cycle. Knaus referred to Fränkel's theory as a misinterpretation. It is, however, neither a misinterpretation nor a mistake, but it corresponds with the facts. The liberation of the second ovum is not violent, provoked, or artificial, nor is it a coincidence; in fact it is quite normal and regular.

From Fig. 1 it is evident how it is that a wrong conclusion has been drawn despite correct observations by the said scientists. If the Graafian follicle ruptures, the corpus luteum forms in the oviduct after about 30 hours. It is capable of changing into a corpus luteum gravidarum within another 30 hours. For nidation occurs, as cyclograms 2, 3 and 4 indisputably show, within a period of no more than 3 days and not after 10 days, as has so far been assumed. If the ovum is not fertilized, after 48 hours it becomes incapable of fertilization. Owing to the absence of the direct impulse of the trophoblast (chorial hormone) of the fertilized ovum and the consequent absence of the luteinizing hormone of the hypophysis, the first corpus luteum does not change into a corpus luteum gravidarum, but is on the contrary arrested in its development and suppressed by the increased follicular production of the ripening second ovum. The increased formation of the luteal hormone and of the luteinizing hormone of the hypophysis arrest the production of the egg-ripening hormone of the hypophysis, the lobus posterior hormone and the folliculin. Inversely the increased folliculin formation of the second ripening ovum suppresses the luteal hormone-formation of the first corpus luteum, not only directly but also indirectly, seeing that during this period the egg-ripening hormone of the hypophysis predominates and the luteinizing hormone of the hypophysis is decreased or checked. In this way the first corpus luteum is suppressed directly by the second ripening ovum and indirectly by the hypophysis.

If the ovaries are examined immediately before or after the

rupture of the first Graafian follicle, only one ovum is found, since the second ovum is not yet developed. When carrying out an examination in the second half of the cycle before or after the bursting of the second Graafian follicle one would expect, if an ovum has already been liberated, to find a formation which resembles a corpus luteum in the other ovary. It should, therefore, be an organ with a diameter of 1 to 1½ centimetres, bluish in colour and projecting beyond the surface of the ovary. Since, however, the scientists did not find such a formation, but, on the contrary, discovered that the surface of the ovary was level, or in some cases even depressed, it did not occur to them that an ovum had been liberated in the other ovary about 6 to 7 days previously. Pathological anatomists who found a regressive, retarded or suppressed corpus luteum were of opinion that this originated during the previous cycle. The scientists did not realize that this undeveloped corpus luteum came from a Graafian follicle which had ruptured only a few days before.

The development of a corpus luteum when the first ovum has not been fertilized would, moreover, be to no purpose at this stage of the cycle. Between two ovulations it may, of course, happen when one is inspecting the ovaries that a recently ruptured Graafian follicle is found in the one ovary and in the other a second ovum in the process of developing, as both Fränkel and Grosser discovered on several occasions when performing abdominal operations. This is especially possible in the case of young nulliparae in whom the period between two ovulations is not about 6 to 8 days, but often much shorter (Fig. 7). The fact that Robert Meyer arrived at varying conclusions proves that it is far from easy to define the time of ovulation by the age of a corpus luteum and to determine whether a corpus luteum is regressive, or whether it has been checked in its development.

Immediately after the rupture of the second Graafian follicle it is only by way of exception that there are clear signs in the other ovary by which it is possible to diagnose a primary ovulation. After the second ovulation a more or less highly developed second corpus luteum menstruale is found. In the event of the ovum being fertilized this corpus luteum changes into a corpus luteum gravidarum in the manner already described. If the second ovum is not fertilized and if a third ovum is not liberated in the same cycle, the production of the egg-ripening hormone of the hypophysis and of the folliculin decreases. In consequence of this there is an increased production of the luteinizing hormone of the hypophysis, which is no longer arrested by the increased

production of folliculin, and the second corpus luteum then begins to develop (Fig. 1).

The previously proliferated endometrium is now transformed by the luteal hormone of the second corpus luteum, and we see the cyclical changes in the endometrium which were first described by Hitschmann and Adler.[13] A study of numerous cyclograms warrant the assumption that it sometimes occurs that when the second ovum is not fertilized the luteinizing hormone of the hypophysis also stimulates the first corpus luteum to form luteal hormone. This accounts for the difference between cycles of 26 to 28 days and those of 30 to 31 days, as explained below.

After developing for a time the second corpus luteum becomes regressive, the luteal hormone formation ceases, and the cells of the endometrium, which are no longer supplied with folliculin and luteal hormone, die. In the case of human beings these cells, after having exfoliated, are cast off to the accompaniment of bleeding, and owing to the predominance of the lobus posterior hormone are forced out of the uterus (menstruation).

All these processes may be followed in the cyclogram (Fig. 1). Menstruation is indicated by the menstruation decline "A". The ripening of the first ovum and the subsequent proliferation of the endometrium are indicated by the pre-ovulation peak "B". The liberation of the first ovum and the duration of its life are expressed by the downward section of the ovulation decline "C", while the rising section indicates that the ovum can no longer be fertilized, and that a second ovum is developing. The second pre-ovulation peak "D" corresponds with the ripening of the second ovum; the liberation of this ovum and the period during which it is capable of being fertilized are indicated by the downward section of the second ovulation decline "E", while the rising section once again indicates that the ovum is no longer capable of being fertilized. The development of the second corpus luteum and the transformation of the endometrium are finally expressed in the pre-menstrual peak "F". After about 4 to 5 days the curve then begins a decline, when the second corpus luteum becomes regressive and the luteal hormone mass decreases. The lowest point of the curve is a sign that the production of luteal hormone has ceased and that the corpus luteum has died. This usually occurs one day before menstruation. After the surface layer of the endometrium has exfoliated and been cast off, accompanied by bleeding, we again see a rise in the curve, for the first ovum in the new cycle is developing and the proliferation of the endometrium commences.

The cyclogram is thus an exact record of the hormone-content of the blood. It indicates with the greatest precision the slightest hormonal changes in the body of a woman, as Fig. 1 decisively proves.

Now we have explained how the various scientists adhered to the one-ovum-per-cycle theory, we shall give indubitable proofs that the regular declines in the curve between the two menstruations are caused by the liberation of two or more ova. These proofs are:

(1) In 4 cases I could indisputably prove that fertilization occurred during both the first and the second declines in the curve (see Figs. 2, 3 and 4).

The gravidity represented in Fig. 2 was treated at length in the *Journal of Obstetrics and Gynaecology*, 1937, xliv, pp. 1041–2. In this case the first ovum was fertilized.

Fig. 3 shows an indisputable fertilization of the second ovum in the case of a woman of 30 years. There is a sharp rise in the curve on the third day. It is possible that the curve in Fig. 2 also rose to the same extent on the third day, but that it so happened that the spectroscopic examination was not carried out at the peak period. In all cases of fertilization we see that on the third day the curves show changes which leave no doubt whatever that contact has been established between the ovum and the maternal tissue.

Cyclogram 4 is particularly interesting. It refers to a woman, 26 years of age, with a cycle of 28 days. She had been married for about a year and believed that she was barren. I dilated the cervical canal and, as the portio was anteverted, I advised the patient to lie face downwards immediately after coition. In this way the patient, whose curve was regularly recorded, was fertilized during the first ovulation. The second ovum did not develop, as is shown in the cyclogram. Menstruation did not take place at the expected time. Twelve days later a miscarriage occurred. Seeing bleeding was profuse I curetted the uterus and with the aid of the microscope I detected decidua and chorionic villi in the discharge. I then advised the patient to take about 6 weeks' rest and to wear a pessarium occlusivum. In the following cycle I allowed the first ovulation to pass, and for a few days I measured her reduction time in the morning and in the evening. At the beginning of the second ovulation decline the patient was advised to have intercourse once only without the pessarium occlusivum. This coition likewise resulted in fertilization, as can be seen in cyclogram 4. The patient was then pre-

scribed chorion powder 3 times a day and she was given injections of 5 rabbit-units luteal hormone every other day for a period of 4 weeks. Gravidity persisted and the patient has now been pregnant for 4 months. The daily reduction figures are, as usual, constant.

It will be seen that in all 4 of the pregnancy cyclograms the curves are about the same: on the third day a sudden rise, then a sharp decline followed by fluctuations, after which the curve becomes constant. These 4 cases indisputably prove that there are two ovulations in each cycle. For the ovum is capable of fertilization for a period of only 2 days. Between the declines in the curve there is almost invariably a space of 6 to 8 days, so that positive fertilization can occur in both instances only when there are two ovulations.

(2) The depressions between the menstrual declines, which are generally to be observed on the ninth, tenth, eleventh or twelfth day and then a second time on the sixteenth, seventeenth or eighteenth day of the cycle coincide with the periods of ovulation recorded by the various scientists (Ruge, Fränkel, Robert Meyer, Schröder, Halban and Köhler, Shaw, Müller, Allen, Grosser, Trippel, Ogino, and others).

These two declines occurred regularly in the case of more than 30 women who were observed, while in the case of numerous young nulliparae three declines were regularly noticed (Figs. 7, 8, and 9). These declines do not occur in cyclograms: (*a*) in the case of men, (*b*) in the case of women after the menopause, (*c*) in the case of pubescent women who have had both ovaries removed by operation (2 cases), (*d*) during pregnancy, when, as is known, menstruation and ovulation are suspended. Both these processes recommence after pregnancy is terminated by parturition or miscarriage.

Accordingly, in the case of pubescent women with functioning ovaries, there must be a process which does not occur in the case of men or in the case of post-climacteric, ovariectomized, or pregnant women. This can only be the process of ovulation. And as there are two or three declines in the curve, the conclusion is justified that they are caused by two or three liberated ova.

(3) If fertilization occurs during the first ovulation there is no second decline in the curve—as is seen in cyclograms 2 and 4. This is in keeping with the known facts that when a woman becomes pregnant the second ovulation is suppressed by the corpus luteum gravidarum and by the predominating luteinizing hormone of the hypophysis. If fertilization takes place during the

second ovulation the cyclogram naturally shows both ovulation declines (cyclograms 3 and 4). This likewise proves that the second decline indicates a second ovulation.

(4) When performing abdominal operations, both after the first and after the second ovulation, I have found that the ovulation decline as diagnosed with the aid of the spectroscope always coincides with the rupture of the Graafian follicle. As has already been explained we must not expect, when performing an operation during the second ovulation, to find a fully developed corpus luteum in the other ovary.

If, however, the process of the suppressed formation of the first corpus luteum described in the beginning of this paper is understood, one often finds indubitable signs in the other ovary that here a Graafian follicle also ruptured a few days previously. This is particularly the case with young nulliparae, in whom there are frequently only 2 to 3 days between the two ovulations (cyclogram 7).

(5) The occurrence of binovular twins proves that more than one ovum is liberated in one cycle. In the case of a nullipara whose ovulations occur at short intervals it is possible that the development of the second ovum is not suppressed by the fertilization of the first ovum, if the nidation of the fertilized first ovum has not yet taken place when the second ovum is liberated and consequently the chorial and luteal hormones do not arrest the development of the second ovum. Binovular twins are possible if a Graafian follicle contains two ova, as has been indisputably proved, or if by way of exception two ova are liberated simultaneously in the same ovary. Binovular twins may, therefore, very well be regarded as a proof that two ova are liberated in one cycle, but not that two separate ovulations take place with an interval of 6 to 8 days in one cycle.

(6) This also applies with regard to superfoetation and superfecundation.

(7) The occurrence of extra-uterine and intra-uterine pregnancies of the same age is another proof of this.

(8) Pregnancy in both horns of a uterus bicornis with foetus of equal age (as I have often seen in big pathologic-anatomical collections) is likewise a proof of this.

The observations submitted *sub* 1 to 8 prove that more than one ovum is liberated in each cycle. The proofs *sub* 1 to 4 may be regarded as absolute, while at the same time they confirm the periods of ovulation indicated by C and E in the cyclogram.

The cyclogram not only indicates exactly the hormonal

changes in the maternal body and provides an absolute proof that two or more ova are liberated in one cycle, but it also shows when a woman is capable of conceiving and when she is sterile (see cyclogram 5).

(1) A woman is most liable to conceive during ovulation, as the ovum is then fertilizable. The possibility of fertilization is greater on the first day *b* to *c* than on the second day *c* to *d*.

(2) Coition 3 days before the ovum is liberated may cause conception because the spermatozoa retain their fertilizing powers for 2 to 3 days (Knaus and others) in the genital tract of the woman (*a* to *b*).

(3) After the second ovulation until 3 days after the beginning of menstruation a woman is absolutely sterile because the ovum has not been liberated. None of the sexually mature women whom I had advised against using contraceptives during this time conceived (*st* to *r*).

(4) Three days after the beginning of menstruation until 3 to 5 days before ovulation the woman is also sterile. This period I call the phase of relative sterility (*r* to *t*) because the various scientists do not agree on the duration of viability of the spermatozoa. Pryll and Nürnberger,[15] for instance, found living spermatozoa in the oviduct as long as 15 days after insemination. Although, practically speaking, it never happens that such spermatozoa will successfully fertilize ova, the above-mentioned period must still be regarded as the phase of relative sterility. In the case of a woman for whom pregnancy is not desirable for reasons of health one extra day must be reckoned for ovulation (*d* to *a*) and two extra days for the viability of the spermatozoa (*t* to *a*), for it is not impossible that by way of exception the ovum and spermatozoa remain capable of fertilization for a longer period than is usual. Cyclogram 5 indicates exactly the periods of conception and sterility. Practically speaking, one may say that during the period marked *x* to *y* in the cyclogram conception is possible and that from *y* to *z* the woman is sterile.

So far it has been assumed that the nidation of the fertilized ovum takes place 10 days after fertilization. This assumption has now become untenable. After a close study of the pregnancy curves in cyclograms 2, 3 and 4 it may be said with certainty that nidation takes place within 3 days after fertilization. After about 72 hours the pregnancy curves in the cyclograms rise to a level which can only be due to an hormonal change in the maternal organism. This hormonal change is brought about by the primary influence of the fertilized ovum. Robert Meyer was right in

concluding that it is the fertilized ovum which primarily causes all changes in the maternal organism. It can, however, only perform this function after the ovum has become attached to the maternal tissue—nidation. It is out of the question that an egg-cell of about 60 microns which is in the oviduct or the uterus, but still unconnected with the maternal organism, can bring about such an hormonal change as is indicated in all pregnancy curves on the third and fourth day.

These changes can only be accounted for if we assume that the trophoblast first forms chorial hormone and that these in their turn exercise a direct and an indirect influence on:

(1) The corpus luteum, which changes into a corpus luteum gravidarum accompanied by an increasing formation of luteal hormone.

(2) The subsequent ripening process of the ovum and the formation of folliculin which are arrested.

(3) The egg-ripening hormone of the hypophysis, which is suppressed and on the luteinizing hormone, which increases.

(4) The lobus posterior hormone, the pituitrin, which it arrests.

All these processes prevent the uterus from contracting, a condition which is essential for the undisturbed development of the fertilized ovum. This quiescence is expressed in the daily unvarying figures in the cyclogram. Quiescence in the cyclogram means quiescence in the hormone readings and quiescence in the walls of the uterus. When pregnancy has taken its normal course, or there is a miscarriage, this quiescence is disturbed and the above-mentioned fluctuations are again observed.

The fact that nidation takes place within 3 or 4 days and not after 10 days is proved by the following:

(1) The sharp rise in the curve on the third day and the subsequent decline on the fourth day after fertilization has taken place. The hormonal changes which are seen in the cyclogram can be taken only as a sign that trophoblast formation has commenced.

(2) Owing to the direct and indirect influence of the fertilized ovum there is no second ovulation decline, which usually takes place 6 to 8 days after the first. Nidation must, therefore, have occurred previously.

(3) The second ovulation usually takes place on the sixteenth, seventeenth or eighteenth day. An ovum liberated on the eighteenth day would, according to the hitherto prevailing opinion, nidate on the twenty-seventh or the twenty-eighth day; in other words, just when menstruation should begin. This,

however, would be against the laws of nature and is, therefore, not acceptable. If nidation really took place after 10 days, the corpus luteum gravidarum would not commence developing until after the twenty-eighth day of the cycle. It could not then arrest the subsequent menstruation. This is contradictory to the observations in cyclograms 3 and 4, when menstruation did not appear after the fertilization of the second ovum. It follows that nidation must have taken place previously.

(4) According to Stöckel,[16] v. Möllendorf,[17] Miller,[18] Bryce-Teacher,[19] Peters,[20] and others, the youngest human ova that have so far been examined were 12 days old. These ova were already surrounded by a strong trophoblast and (according to Stöckel-Linzenmeier[21] and Bryce-Teacher) were completely embedded in the endometrium, so that the nidation process had presumably commenced several days previously.

(5) When a miscarriage occurred after 12 days I detected young chorionic villi in the coagula (see *The Journal of Obstetrics and Gynaecology*, 1937, xliv, pp. 1036–55).

The most conclusive proof is furnished by the above-mentioned changes in the pregnancy curves on the third or the fourth day (Figs. 2, 3 and 4).

One of the most important phases in the cycle is menstruation. It is most easily defined by a description of the processes:

Menstruation is a periodical dying-off of the surface layer of the endometrium due to the withdrawal of folliculin hormone and subsequently of luteal hormone, followed by desquamation and discharge of the necrotic cell tissues accompanied by bleeding of the hyperaemic basal layer.

The basic factor here is the dying-off of the endometrium upon the withdrawal of hormone, to which these cells are very susceptible. The higher the hormone readings are and the lower the level to which they subsequently decline the more quickly the cells die off, which process is usually but not always in keeping with the intensity of the bleeding. This withdrawal of the hormone is brought about by the regressive corpus luteum, which inhibits the formation of luteal hormone. This in turn is caused by the fact that fertilization has not taken place.

The endometrial cells do not always die on this account; sometimes the dying is due to a sudden withdrawal of folliculin or a sudden change from folliculin to luteal hormone.

An example that bleeding of the endometrium can also occur after a sudden withdrawal of folliculin alone is shown in cyclograms 7 and 9. Fig. 7 represents the cyclograms of 3 consecutive

months of a girl, 15 years of age, who menstruated fairly regularly every 30 days. In the interval between the flows, however, there was bleeding during the first and again during the third ovulation. These bleedings I term ovulation bleedings. In the cyclogram we see that such bleeding occurs when there is a sudden big drop in the curve in a single day. It mostly occurs when the declining curve approaches its lowest point, but may occur 1 or 2 days later. The latter case can be accounted for by the fact that in certain instances the coagula are not immediately discharged from the narrow ostium of the nullipara. The young girl also mentioned that the bleeding usually begins with pink discharge and that later she gets abdominal pains attended with the passing of black clots of blood. This agrees with the supposition that the blood is subsequently forced out of the narrow ostium to the accompaniment of painful contractions of the uterus. In the first month we see an ovulation bleeding such as the French call *crise intermenstruelle* during the third ovulation. In the second month there is an ovulation bleeding during the first and second ovulations and in the third cycle again during the third ovulation. In the last instance bleeding did not begin until one day after the lowest point had been reached. In all 4 cases of ovulation bleeding we see a sudden big decline in a single day, very often recording a difference of more than 30 seconds in the cyclogram. During the first ovulation bleeding there cannot as yet be any question of a corpus luteum. It can, therefore, only have come about as a result of a sudden withdrawal of folliculin. This is the first time that it has been possible to represent such a process graphically and bring it, as it were, *ad oculos*. That a sudden withdrawal of folliculin can lead to the death of the proliferated endometrium is incidentally proved by the experiments of C. Kaufmann,[22] which I can confirm. If women are given large quantities of folliculin after the menopause and the supply is then suddenly stopped, the endometrium dies to the accompaniment of bleeding the following day or a few days later. I have made the same observations repeatedly in the case of women who were suffering from secondary amenorrhoea.

It is probable that a sudden change from luteal hormone to folliculin is also capable of causing bleeding, as is pointed out in the explanation of the difference between cycles of 26 to 28 days and those of 30 to 31 days. That the bleedings generally become more profuse as the hormone reading rises, that is as more hormone enters the cells before its withdrawal, is demon-

strated by the cysto-glandular hyperplasia of the endometrium. As I was able to prove with the endocrine electro-diagram,* there is a hyperpituitarismus and a hyperfolliculinaemia, that is to say, over-function of the hypophysis and the ovaries. Under the influence of the hyperfolliculinaemia an abundant proliferation of the endometrium and of the myometrium sets in. This in its turn leads to menorrhagia. A correct diagnosis of these processes made it possible for the first time to cure with organo-short-wave therapy cases of cysto-glandular hyperplasia, which are often accompanied by all kinds of disturbances of the diencephalon.* [25]

As already demonstrated at the Congress at Utrecht (Holland) and at the International Short-wave Congress in Vienna, there is primarily an under-function of the hypophysis and secondarily an under-function of the ovaries in the primary and, as a rule, also in the secondary amenorrhoea; in the case of cysto-glandular hyperplasia we are concerned with a primary over-functional hypophysis and a secondary over-functional disturbance of the ovaries.* [25]

If the hormone is withdrawn slowly, it may happen that the cells of the endometrium do not die and that bleeding is absent, as can be seen in cyclogram 7, especially in the third month, where the first two ovulation declines take 2 days each and the third sharp ovulation decline, which takes place in a single day was accompanied with bleeding.

In case of hormonal change, where the quantities of luteal hormone gradually decrease and the supply of folliculin gradually increases (Fig. 8) it may happen that the endometrium is able to recover without desquamation and bleeding, as in the case of animals. This process, which can be observed in the cyclograms (Figs. 8 and 9) in cases of patients suffering from amenorrhoea, where the graph shows a rudimentary decline I have, therefore, called an animal menstruation. The menstruation curve then shows either a gradual and steady decline (Fig. 8) or only a very slight one (Fig. 9).

Fig. 8 is the cyclogram of a girl, 18 years of age, who has not menstruated for 4 months. She is a little anaemic but is otherwise healthy and has, probably because of a natural tendency strengthened by the anaemia, an over-function of the hypophysis and of the ovaries, a fact which could be proved by an analysis

* See Report of J. Samuels, Medical Congress, Utrecht, 1937, and Report of International Short-wave Congress, Vienna, 1937.

of the endocrine system. This in itself diminished the supply of hormone to the endometrium. The endometrium grows accustomed to small quantities of hormone and, the corpus luteum having become regressive, is gradually supplied with folliculin, as a result of which it does not die and menstruation does not occur.

Still more interesting is cyclogram 9, which was made of an apparently healthy young girl of 17 years. At first we see a normal menstruation decline with a normal menstrual flow, and after 28 days a rudimentary menstruation decline during which there is not any discharge. The curve then rises to the pre-ovulation level in preparation for the first ovulation in the new cycle. During the first ovulation there is ovulation bleeding, and we once again see the sudden big drop in a single day with which these ovulation bleedings are attended.

In treating secondary and, above all, primary amenorrhoea the cyclogram now shows the way and indicates the stage of the cycle at which the patient has arrived. Formerly a solution could not be found to this problem. Neither was it known whether such a patient ovulated or not. But it is not only of importance to science to know the cycle-phase of the patient suffering from amenorrhoea; it has also a practical therapeutic value, for it is a matter of great importance in which phase of the cycle we apply therapy. I succeeded, for the first time, in curing a case of primary amenorrhoea, a malady which used to be regarded as incurable (Clauberg,[23] Kehrer,[24] Kaufmann and others), by means of organo short-wave therapy. With the aid of folliculin we cause the development of the hypoplastic uterus and with the short-wave therapy of the endocrine system* which I have devised, we restore the equilibrium between the under-functioning hypophysis and the ovaries. The patient in question is a girl of 23 years of age who has menstruated regularly 10 times every 28 days since the beginning of the treatment, and it can be proved that she ovulates regularly twice a month.

Cyclograms 8 and 9 also show in which phase the patients are who do not menstruate. Without the cyclogram there would be no indication of this. Therefore, if all kinds of irregularities connected with menstruation are in future to be diagnosed and treated correctly cyclograms or the endocrine electro-diagram, which enables us to analyse the endocrine system will be indispensable. It is not only as regards every normal woman but

* See reports of congresses at Utrecht and Vienna, 1937.

also in the case of these patients suffering from amenorrhoea that we observe a first pre-ovulation peak, the first ovulation decline, the second pre-ovulation peak and the second ovulation decline, and in the case of young nulliparae, in whom there is a third ovum, also a third pre-ovulation peak and a third ovulation decline—and, finally, the pre-menstruation peak with the subsequent rudimentary menstruation decline. (Compare Figs. 1 and 5 with 8 and 9.)

The numerous cyclograms of women with a cycle of 26 to 28 days and of those with a cycle of 30 to 31 days justify the assumption that in the case of a cycle of 30 days and more the menstrual flow does not occur on the twenty-eighth day because the two corpora lutea do not become regressive simultaneously. They also justify the assumption that if the second ovum has not been fertilized, the subsequently predominating luteinizing hormone can incite the first corpus luteum to form luteal hormone. On comparing the graphs of women with a cycle of 26 to 28 days with those of women with a 30 to 31-day cycle we find that in the case of the first-mentioned group the curve usually reaches its lowest point on the twenty-eighth day (Fig. 5). Menstruation begins on the following day. The low level of the curve shows that the formation of luteal hormone has been arrested, whereupon the endometrial cells die. In the cyclogram of women with a cycle of 30 to 31 days (Fig. 6) we also generally find the lowest point of the curve on the twenty-eighth day.

According to what is so far known and according to the results of the animal-biological tests made by Frank,[25] of New York, to determine the quantity of hormone present in the blood one would think that also in this instance menstruation would begin the next day. This, however, is not the case. Menstruation does not begin until 3 or 4 days later, when the curve has already risen to a certain level (Figs. 6 and 7). On the two subsequent days the curve again declines a little and then rises—just as in the case of the other group—to the pre-ovulation level of the new cycle. Fig. 6 shows that the graphs of both types of women touch the lowest point on the sixteenth day after the first ovulation decline and that menstruation begins on the fourteenth day after the second ovulation decline. The duration of the life of the corpus luteum of human beings has hitherto been assumed to be 14 to 16 days, or, according to Ogino, 13 to 17 days. According to my studies of cyclograms, however, the corpus luteum menstruale continues to exist 19 to 9 days after the liberation of the first and second ovum respectively, a latent period of

usually 4 to 8 days having to be taken into account for the first corpus luteum.

The observation that in the case of a cycle of 30 to 31 days the lowest point is reached 13 to 17 days after the first ovulation, whereas menstruation and the second lowest point occur within 13 to 17 days after the second ovulation justifies the conclusion that the corpora lutea of the first and second ovulation become regressive one after the other, whereas in the case of women with a cycle of 26 to 28 days both corpora lutea are regressive at the end of the cycle, when menstruation begins. It is quite possible that the first corpus luteum did not develop at all, or that it developed and then perished together with the second corpus luteum. Occasionally, though not often, it happens that the graph of a woman with a 28-day cycle shows features similar to those seen in the graph of a woman with a cycle of 30 to 31 days. If in the case of such a woman the lowest point of the curve does not as usual coincide with the beginning of the menstruation it is reached within 13 to 17 days after the first ovulation, and menstruation also begins within 13 to 17 days after the second ovulation decline. Among the numerous women with a 28-day cycle whom I have so far examined I met this but once, the first ovulation taking place on the eighth day and the second on the fourteenth day, the biggest drop being on the twenty-fourth day and the beginning of the menstruation on the twenty-eighth day. Unfortunately, I had no opportunity of following up this curve in subsequent months. It is not improbable that if the ovulation occurred at a later period it changed to a 30 to 31-day cycle in the following month. Such a change of cycle often occurs, especially after a miscarriage or parturition. Whether this difference must be attributed to a more abundant production of luteinizing hormone of the hypophysis in women with a cycle of 30 to 31 days could perhaps be ascertained by means of comparative biological tests designed to determine the quantity of hormone in the blood.

From the cyclograms it can be seen that the surface cells of the endometrium possess the specific quality that they are only able to exist with a sufficient supply of folliculin or luteal hormone and that they die off when these hormones are withdrawn. If the supply of hormone is excessive—as, for instance, in the case of cystoglandular hyperplasia—hypertrophy of the endometrium begins. This fact is probably of importance in connexion with cancer aetiology, as will be explained later.

SUMMARY.

(1) A sexually mature woman ovulates twice in each cycle; young nulliparae three times.

(2) The ripening of the second ovum suppresses the formation of the corpus luteum of the first ovum by means of hormone. Because of this all scientists who have carried out examinations during the second half of the cycle diagnosed only one ovulation.

(3) The human ovum is capable of fertilization for at most 2 days.

(4) Nidation takes place within three times 24 hours after fertilization, as all early pregnancy cyclograms indicate (Figs. 2, 3, and 4).

(5) The surface cells of the endometrium die to the accompaniment of bleeding when there is a sudden change or withdrawal of hormone. These cells usually die as a result of the withdrawal of luteal hormone, but it is certain that a sudden cessation of the supply of folliculin can also cause this.

(6) Bleeding may also occur in the case of young girls during an ovulation as the result of a sudden and sharp decline in the curve (Fig. 7). It may also occur when large quantiies of folliculin are supplied to the endometrium and then suddenly withdrawn. A corpus luteum and luteal hormone are not essential to desquamation with bleeding. When the hormonal changes are slow the endometrium can recover without bleeding.

(7) The mucous membrane is transformed by the second corpus luteum menstruale.

(8) Cyclograms tend to prove that in all probability predominating luteinizing hormone of the hypophysis may also incite the first suppressed corpus luteum to form luteal hormone after the second unfertilized ovum has died. The cycle takes 26 to 28 or 30 to 31 days according as the corpora lutea degenerate simultaneously or one after the other.

(9) The possibility of fertilization is greatest during the ovulation decline and the 2 to 3 days preceding it. On the third day after the beginning of the ovulation decline the possibility of fertilization is only very slight; thereafter fertilization is impossible.

A woman is absolutely sterile for 3 days after the second ovulation decline until 2 to 3 days after menstruation begins. After this she is relatively sterile until 3 days before the first ovulation decline (see cyclogram 5). Practically speaking it

may be taken that a woman is capable of conceiving from X to Y and sterile from Y to Z.

(10) The cyclogram accordingly serves as a guide in determining all processes of ovulation and conception and in diagnosing and treating all irregularities in menstruation.

The cycloscope* (Fig. 10) will, therefore, prove to be an indispensable instrument not only for the gynaecologist but also for all general practitioners.

* Obtainable from Anderson and Polak, P.C. Hooftstraat 40, Amsterdam.

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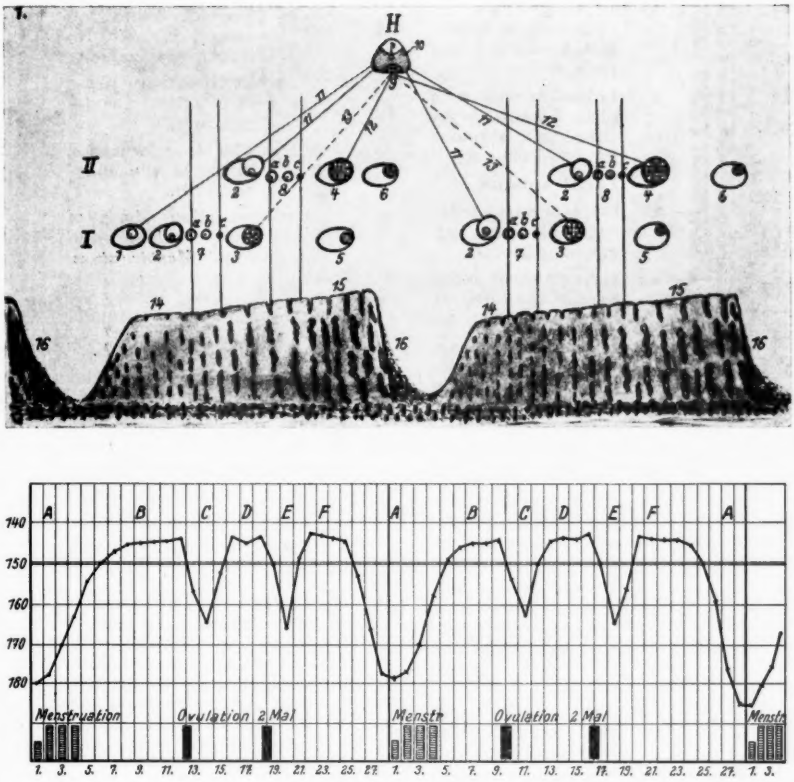


FIG. 1.

DIAGRAM SHOWING THE HYPOPHYSARY INFLUENCES OF THE OVULATION PROCESS OF THE ENDOMETRIUM AND THEIR RELATION TO THE CYCLOGRAM.

Explanation of Fig. 1.

Diagram

H = Hypophyse.

9 Place where luteinizing hormone forms (prolan B).

10 Lobus anterior with place where egg-ripening hormone forms (prolan A).

P Lobus anterior.

— 11 Hypophysary influence of the egg-ripening process.

—— 12 Hypophysary influence of the luteinizing process.

- - - 13 Luteinizing suppressed by the folliculin production of the ripening second ovum.

1 Ovary with ripening Graafian follicle.

2 Ovary with Graafian follicle immediately before rupturing.

3 *Corpus luteum* formation *suppressed* after the first ovulation by the growth of the second ovum.

4 Corpus luteum of the second ovum fully developed.

5 Regressive corpus luteum of the first ovulation.

6 Regressive corpus luteum of the second ovulation.

7 (*a*) First ovum on first day. (*b*) First ovum on second day. (*c*) No longer fertilizable.

8 (*a*) Second ovum on first day. (*b*) Second ovum on second day. (*c*) No longer fertilizable.

14 Proliferation phase of the endometrium.

15 The transformation phase of the endometrium.

16 Secretion phase of the endometrium resp. *Menstruation*.

Cyclogram

Menstruation.

Ovulation (twice).

A Menstruation decline.

B First pre-ovulation peak.

C First ovulation decline.

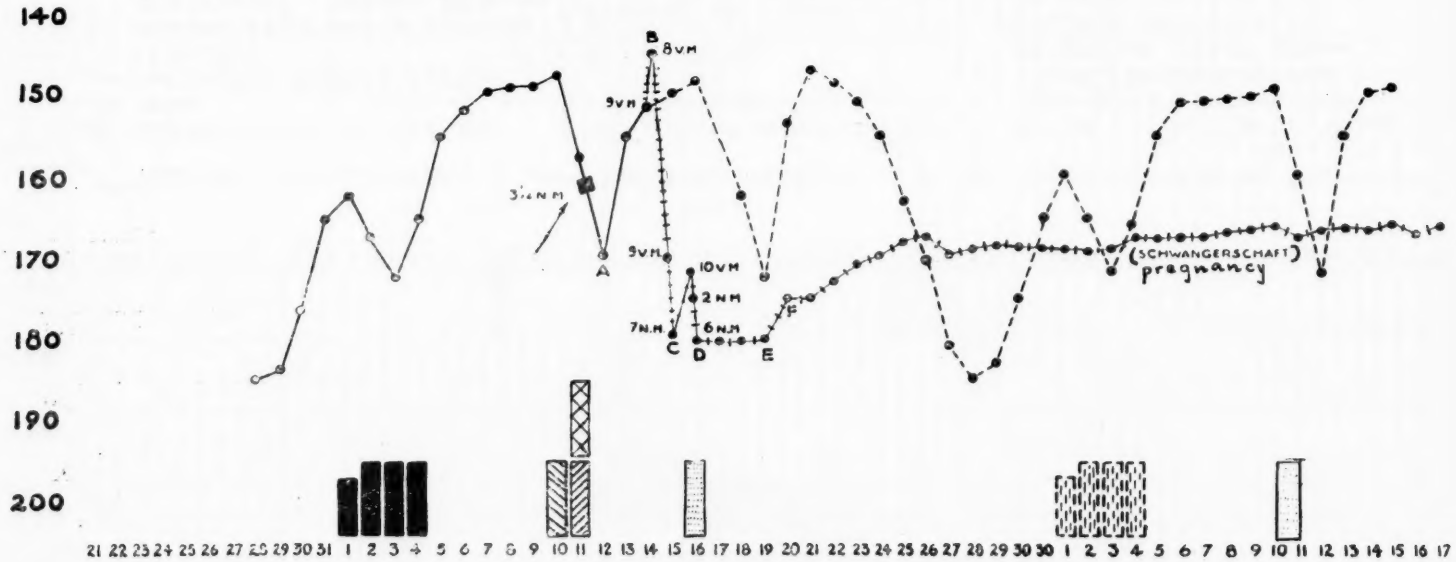
D Second pre-ovulation peak.

E Second ovulation decline.

F Pre-menstruation peak. Note the difference between the first month (ovulation on the twelfth and eighteenth days) and the second month (ovulation on the ninth and sixteenth days).

All stages of the egg-ripening and luteinizing processes and the various phases in the development of the endometrium are given in the cyclogram, which may be taken as an exact recording of the *hormonal* changes in the blood.

FIG. 2. CYCLOGRAM BEFORE AND AFTER FERTILIZATION. CYCLE 31 DAYS (THE CYCLE OF THE PRECEDING MONTH IS SCHEMATIZED FOR THE PERIOD AFTER FERTILIZATON).



Menstruation

1st Ovulation day

2nd Ovulation day

Schematized ovulation day if no fertilization had taken place

Copulation 3 1/2 h.p.m.

Fertilization

—Cyclogram until changed through fertilization

---Cyclogram of the preceding month schematized in month of fertilization

Change of cycle through fertilization.

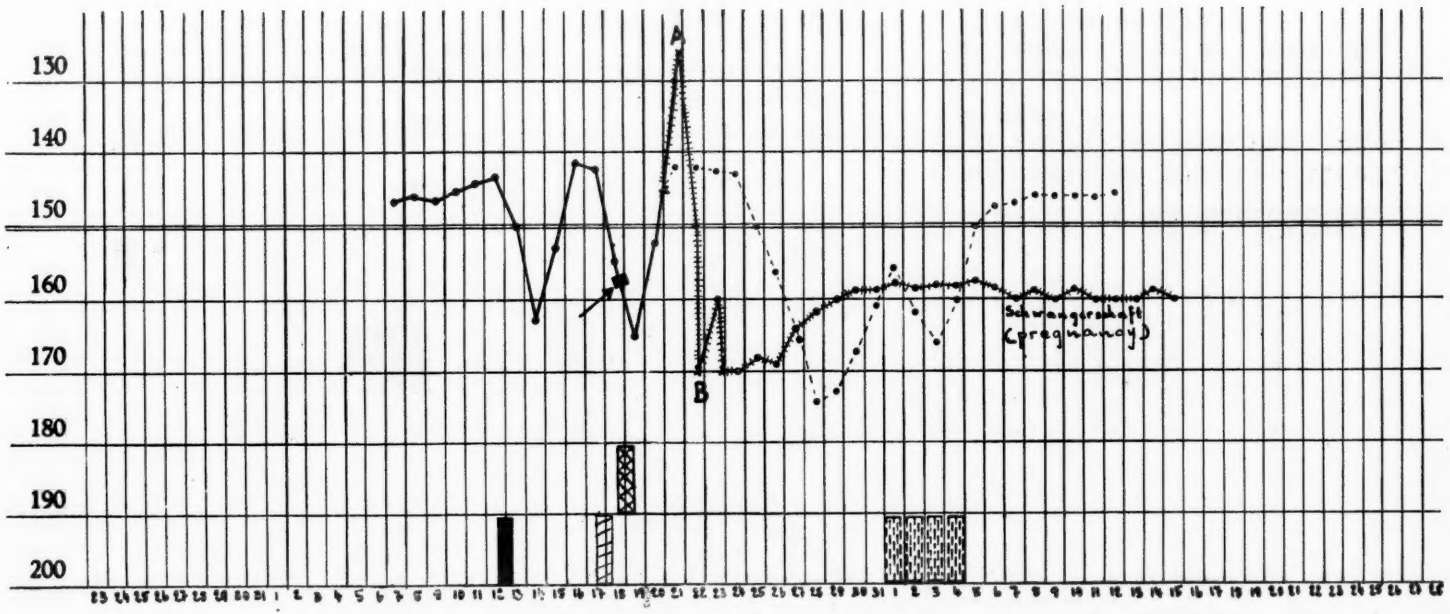
Schematized menstruation if no fertilization had taken place.

No menstruation occurred. 10 days later Friedemann reaction positive.

3.

CYCLOGRAM

of fertilization after the 2nd ovulation – cycle 31 days



1st ovul. 2nd ovul.

Copulation at 5 p.m. +++ Pregnancy curve

Impregnation of the 2nd ovum

The absent menstruation schematized

—— Cyclogram before fertilization

--- Schematized curve showing the approx. course when no fertilization occurs during a 31-day cycle.

• Day reading

× Reading at 9 p.m.

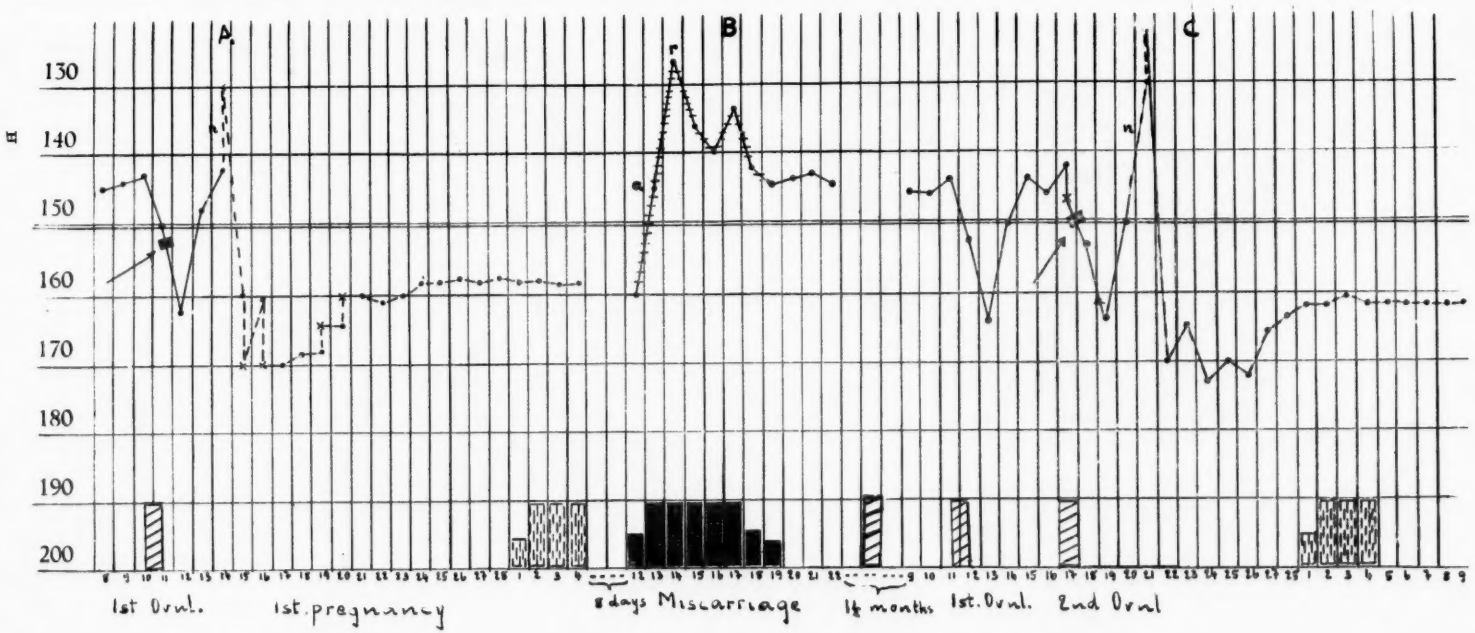
A. Nidation on 3rd day

B. Sharp decline on 4th day. After a few fluctuations the curve becomes constant. Pregnancy was diagnosed after gynecological examination. No menstruation for 3 month.

fertilization occurs during a 31-day cycle.

A. Nidation on 9th day

5 month.



Ovulation

Bleeding

Schematized menstruation if no fertilization occured

Coition

—— Normal curve

--- Pregnancy

• Day reading

× Evening reading

Miscarriage

Miscarriage

r Curetted womb

n Nidation

A/ Fertilization after the 1st ovulation.

B/ Miscarriage; Chorion villi and decidua found

C/ Fertilization about 1½ months later after the 2nd ovulation.

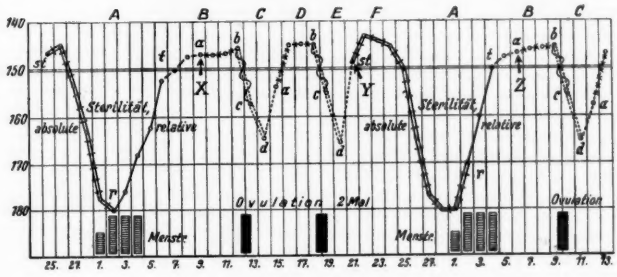


FIG. 5.

CYCLOGRAM OF THE PERIODICAL FERTILITY.

Menstruation.

Ovulation (twice).

A Menstruation decline.

B First pre-ovulation peak.

C First ovulation decline.

D Second pre-ovulation peak.

E Second ovulation decline.

F Pre-menstruation peak.

b–c–d CONCEPTION.
Because the liberated ovum is fertilizable for 2 days.

b–c Possibility of fertilization greatest on the first day.

b–a CONCEPTION.
Because spermatozoa ejaculated during this period may fertilize an ovum liberated later, seeing they remain capable of fertilizing for 3 days.

d–a CONCEPTION DOUBTFUL.
d–st Because the ovum is seldom fertilizable on the third day.

st–r ABSOLUTE STERILITY.
Because there is not any ovum present; this period is longer in the case of a 31-day cycle; in the case of young nulliparae with 3 ovulations often shorter.

r–t RELATIVE STERILITY.
Because scientists such as Nürnberger and Pryll have found living spermatozoa in the tractus genitalis as long as 15 days after insemination.

t–a STERILITY DOUBTFUL.
Because in view of the foregoing it is advisable, by way of precaution, to assume that the period during which spermatozoa are capable of fertilizing is 2 days longer.

It will be observed that in the first month the first ovulation decline begins on the twelfth day and in the second month on the ninth day!

FROM X–Y one should, practically speaking, always reckon on the possibility of fertilization.

FROM Y–Z the woman is practically sterile.

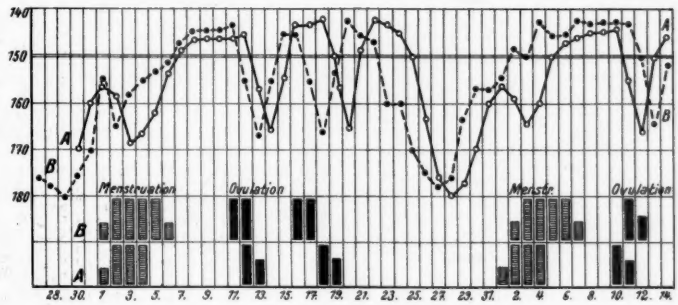


FIG. 6.

CYCLOGRAM OF TWO WOMEN WITH CYCLES OF 31 DAYS.

—— A Represents the cycle of a young married woman of 28 years, nullipara.

—— B Represents the cycle of a young married woman of 27 years with 2 children.

Menstruation (above: patient B). (below: patient A).

Ovulation (above: patient B). (below: patient A).

Note the similarity and the difference between the two curves, in which the main characteristic features are the same, but in which the minor details differ. The difference between the cycle of the first month and that of the second month in the case of patient B is particularly interesting. Compare also these two curves with that of a woman with a 28-day cycle and observe the difference! (Diagrams.)

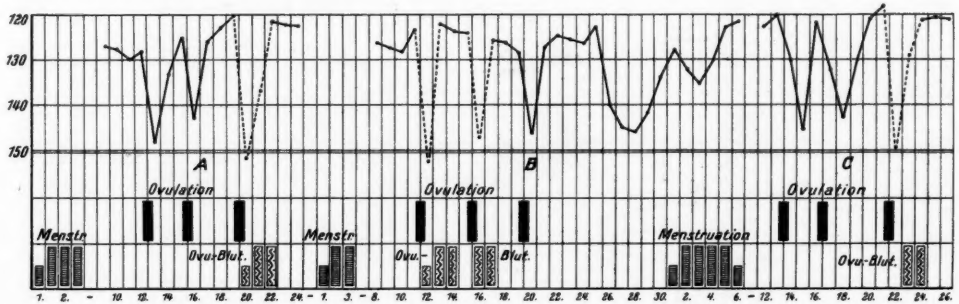


FIG. 7.

CYCLOGRAM OF A FULLY DEVELOPED GIRL OF 15 YEARS WITH MENSTRUAL AND OVULATION BLEEDING.

Recording of the ovulation periods in the course of 3 months (A, B, C).

Menstruation.

Ovulation (3 times).

Ovulation bleeding.

—— Cycle 3 days.

- - - Ovulation decline with bleeding.

A Menstrual bleeding and ovulation bleeding on the twentieth, twenty-first, and twenty-second day of the cycle during the third ovulation.

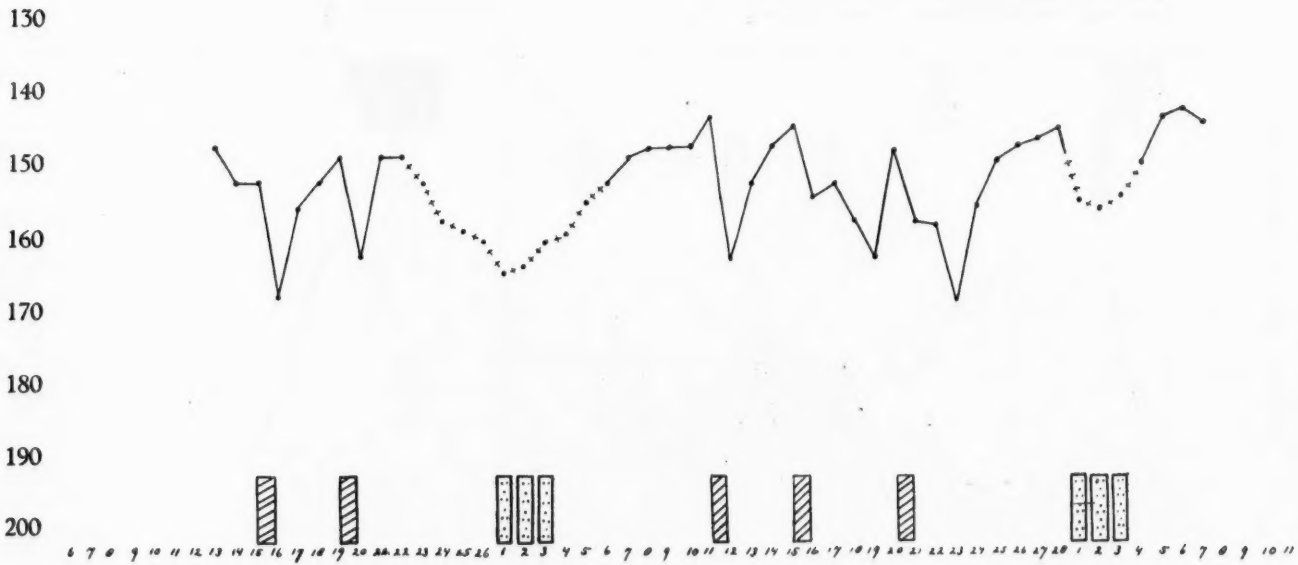
B Menstrual bleeding and ovulation bleeding on the twelfth, thirteenth, and fourteenth day during the first ovulation and on the sixteenth and seventeenth day during the second ovulation.

C Menstrual bleeding and ovulation bleeding on the twenty-third and twenty-fourth day of the cycle after the third ovulation (twenty - first / twenty - second day).

It will be observed that when there is a sharp ovulation decline in a single day ovulation bleeding occurs; when the decline is spread over two days there is not any bleeding.

CYCLOGRAM

of a 16 year old girl with secondary amenorrhoea (animal menstruation)



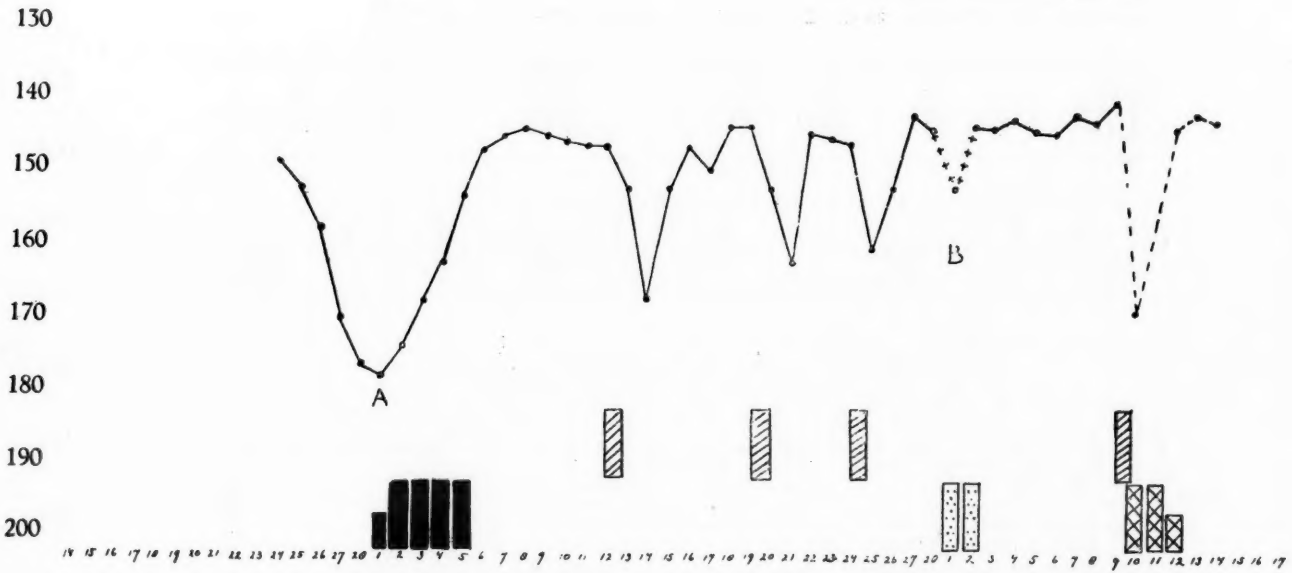
Absent menstruation schematized.
Ovulation (3 times)
—— Cycle curve
****Rudimentary menstrual decline

Patient suffered from anaemia and secondary amenorrhoea. The last discharge 3 months previously. The patient had also menstruated irregularly in the past.

9.

CYCLOGRAM

of a 17 year old girl with a normal, an animal (rudimentary) menstruation and ovulation bleeding in the following cycle.



Menstruation
Ovulation 3 times
A- normal menstruation decline
B- rudimentary cycle decline
Absent rudimentary schematized
Ovulation bleeding
Ovulation decline with bleeding

Patient has a 28-day cycle. The last menstruation persisted for 5 days, 28 days later no menstruation. This was succeeded by ovulation bleeding on the 38th day after the last menstruation. Note the difference in the course of the cycle with the normal and the animal rudimentary menstruation.

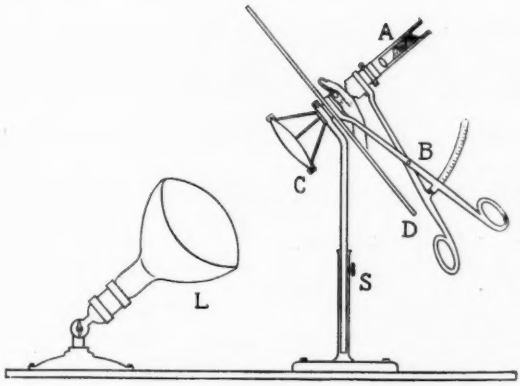


FIG. 10.

CYCLOSCOPE.

A=Spectroscope C=Lens
B="Pincette" L=Light
S=Pedestal.

BRITISH COLLEGE OF OBSTETRICIANS AND GYNAECOLOCISTS

THE Quarterly Meeting of the Council was held in the College House on Saturday, 29th January 1938, with the President, Sir Ewen Maclean, in the Chair.

The following was admitted to the Fellowship:—

Grace Stapleton	New Delhi, India

The following was admitted to the Membership:—

Allan Frederick Hollinrake	Hamilton, Canada

The following were elected to the Membership:—

Yeshwant Narayen Ajinkya	India
John James Armitage	Salisbury
Elinor Francis Elizabeth Black	Canada
Doris Barbara Brown	Harrogate
William Deans Brown	London
William Davies Cunningham	Australia
Mary Evans	Manchester
Martin Birks Hallam	Manchester
Ockert Stephanus Heyns	Manchester
Fergus Duncan Johnston	Canada
John Cameron Loxton	Australia
Benjamin Edward Meek	Canada
John Miller	Greenock
Edward Brettingham Moore	Tasmania
Susanne Jean Paterson	Edinburgh
Robert William Nichol	London
Charles Guy Roworth	Aberdeen
Linton Morris Snaith	Manchester
David Fox Standing	South Africa
Dorothy Marian Stewart	London
Robert Atkinson Tennent	Glasgow
Geoffrey Ashburton Thompson	Australia
William Howie Tod	Leeds
Clifford Vincent Ward	Canada
John Clinton Whyte	Canada
Alice Woodhead	Canada

The President has been appointed to represent the College on the Royal Commission on the Geographical Distribution of the Industrial Population.

The name of Mr. Harold Burt-White has been restored to the roll of Members of the College.

Mr. J. Bright Banister has been appointed to represent the College on the Council of the Queen's Institute of District Nursing.

BRITISH COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

March 23rd, 1938

The following candidates have been awarded the Diploma of the College (23rd March, 1938):—

B. H. Bakewell
S. G. Baldwin
V. M. Crosse
J. C. C. Dawson
F. L. Firkin
J. W. Hannay
J. C. Harvey
H. S. Lanceley
G. S. Lester
H. G. Miller
G. D. N. Milne
H. G. Rees
S. R. Saunders
S. Shrikhande
W. J. Stokes
M. Thomas

SECOND ALL-INDIA OBSTETRIC AND GYNAECOLOGICAL CONGRESS

THE Second All-India Obstetric and Gynaecological Congress will be held at Bombay from the 13th to 16th April 1938. A Medical Exhibition is also arranged as part of the programme.

Subjects selected for official discussions are TOXAEMIA OF PREGNANCY and CARCINOMA OF THE CERVIX.

The Congress will be inaugurated by the Prime Minister, the Government of Bombay, and the Medical Exhibition will be declared open by the Minister of Health.

Dr. B. D. Mukherji, of the Carmichel College, Calcutta, has consented to preside.

All obstetricians and gynaecologists are requested to attend the Congress.

Further information can be obtained from the Organizing Secretary, RAJ BHUVAN, SANDHURST ROAD, BOMBAY, 4.

BOOK REVIEWS

"A Manual of Obstetrics," by T. Watts Eden and Eardley Holland. Eighth edition, 1937. J. and A. Churchill. Price 24*s*.

Since its first edition in 1906 Eden's "Obstetrics" has been rightly regarded as one of the classics of British literature on the subject. Successive editions have been published at intervals of from 2 to 6 years, and each has shown improvement on its predecessor. The new edition, just published, probably shows greater changes than any previous edition, and at the outset it can be truthfully said that this is the best ever. Many of the old illustrations have been replaced and there are three new plates.

The book, as in the previous editions, is divided into sections on Normal Pregnancy; Abnormal Pregnancy; Normal Labour; Abnormal Labour; The Puerperium; The Newly Born Child; Injuries, Diseases and Death of the Foetus; and Obstetric Operations; and each section shows evidence of thorough revision and of having been brought completely up to date.

An excellent and simple account of the endocrine control of reproduction is probably the outstanding feature of the first section of the book, and any student or practitioner reading this intelligently cannot fail to gain an adequate working knowledge of hormonal activity. The dietetic requirements of the mother during pregnancy receive the attention they deserve, and the physiological changes in the urinary system are well portrayed in the light of recent researches.

The treatment of the toxaemias of pregnancy is a section especially deserving of praise, and the treatment, as outlined, is dogmatically and yet accurately stated. An excellent discussion on the anaemias of pregnancy is incorporated, and the section on the subject of urinary infections is considerably altered in conformity with the recent advances made. Vitamin deficiency and hormonal malfunction are considered concisely in their relation to the subject of abortion.

There is little change in the section dealing with the mechanism of labour, but in that dealing with the management of labour notable changes are evident in the sections on the conduct of labour and on obstetrical anaesthesia. The new drug, ergometrine, finds strong favour with the authors.

Haemorrhage due to placenta praevia and accidental haemorrhage are considered separately, and one notable omission in this respect is the lack of reference to Sir Comyns Berkeley's admirable paper on placenta praevia read at Melbourne in 1935.

The practice of trial labour is strongly supported, and the section on uterine inertia is one of the best treatises on the subject yet published in a textbook. The work of Caldwell and Moloy, of New York, on contracted pelvis is well outlined.

In the section dealing with the puerperium and puerperal sepsis one is surprised to find little reference to the Final Report of the Departmental Committee on Maternal Mortality, which by many is regarded as the most

important contribution to the subject yet published. It is mentioned in the guide to further reading. The recent work on the grouping of the various strains of haemolytic streptococci is clearly outlined, and treatment by the prontosil group of drugs is clearly portrayed.

The subject of asphyxia neonatorum and its treatment, especially by intratracheal insufflation, is fully considered, and the section on injuries and diseases of the foetus has gained much in clarity.

In the section dealing with obstetric operations, the relative merits of the classical and the lower-segment Caesarean operations are fairly considered, and a new series of illustrative plates is incorporated. The illustrations showing the application of the forceps in the left lateral position have been omitted.

Dr. K. H. Tallerman has almost entirely re-written the section dealing with the new-born child.

Altogether, Eden's and Holland's "Obstetrics" has gained much by this new edition. The volume is beautifully produced and is almost entirely free from typographical errors. The text is clear and the illustrations excellent. In no place is there any ambiguity and the reviewer found it most readable. It is certainly up to date in every respect, and will undoubtedly retain its position in the forefront of British textbooks of obstetrics.

C.D.R.

"Textbook of Gynaecology," by WILFRED SHAW, M.D., F.R.C.S., F.C.O.G. Second edition, 1938. London: J. and A. Churchill. 616 pages. Price 18*s*.

The fact that a second edition of Wilfred Shaw's "Textbook of Gynaecology" has been called for within two years of its first appearance is sufficient evidence of the position which it has gained for itself as an exposition of this subject.

One of the greatest difficulties in compiling a textbook of this sort, which is directed mainly at the undergraduate preparing for his final examination, is to treat the various aspects of the subject in proper perspective: that has been well done in this case, although Mr. Shaw might have been excused if he had elaborated his account of endometrial and ovarian pathology with which his name is associated.

The arrangement of the book is on the usual lines, and after an account of the structure and physiology of the female pelvic organs, the main gynaecological symptoms, such as pain and discharge, are considered.

The clinical examination of the patient is then considered in detail, but is it correct for the author to say on page 107 that vaginal examination is usually made, in this country, in the left lateral position, especially when, a few pages further on, a diagram is reproduced showing bimanual examination with the patient on her back?

Injuries and diseases of the various areas are then considered systematically, and with most of the author's views there will be general agreement. We would particularly agree with his advocacy of slow drainage of the bladder in cases of incarcerated retroflexed gravid uterus, and the effect of this alone producing spontaneous cure of the condition.

The account of sterility is very good, but surely a more simple apparatus than that of Provis (Fig. 81) suffices for tubal insufflation: Bonney's instrument, much simpler, is equally effective.

It is difficult to justify the inclusion of a chapter on abortion in a gynaecological work, while hydatidiform mole can be justified only on account of the frequency with which it is followed by chorion-epithelioma. In discussing tubal gestation the common error is perpetrated of emphasizing the acute haemorrhagic clinical picture, while the more common sub-acute slowly leaking case with insidious symptoms and signs is not sufficiently stressed. The account of the universal condition of cervicitis and its treatment is properly full, as is the following section on uterine displacements.

In a work of this kind a technical discussion on the relative value of alternative operative procedures can hardly be expected, but we must take exception to the statement on page 405 that complete procidentia cannot be cured by Fothergill's operation. We can assure the author that many hundreds of cases of complete procidentia have been completely and permanently cured by this operation, and that hysterectomy, except for some such local condition as a fibroid, is unnecessary.

The later sections on uterine and ovarian tumours are extremely comprehensive, and the views put forward as regards pathology and treatment are essentially sound.

The format of the book is all that could be expected from Messrs. Churchill, while the illustrations, including so many from Peham, Amreich, and Veit-Stoeckel, are excellent. The illustration, however, on page 727, of Bartholin's cyst is poor and should be replaced in a future edition.

Authorities are not extensively quoted, and it is perhaps regrettable that such references are mainly to foreign sources: in particular it is regretted that the name of Teacher does not appear anywhere in the account of chorion-epithelioma. Time flies, and we are so soon forgotten!

A most useful chapter is that on hormone treatment in gynaecology, while the appendix of preparations is also of value.

It will be appreciated, we hope, that such criticisms as have been made are of detail, and are, therefore, personal. Our opinion of the book as a whole is that it is a first-class and lucid presentation of sane and sound gynaecological practice of to-day, and that it marks the author as a distinguished teacher and a clinician of a high order.

The work will, doubtless, continue its wide appeal, and further editions are certain to be required.

Gilbert I. Strachan.

"Handbuch der Gynäkologie," by Dr. Paul Diepgen. (Part 1), 321 pages, 64 illustrations. München, 1937. Published by J. F. Bernmann.

This book is remarkable, not only for its specialized contents, but for the profound understanding which is displayed by the author in his dealing with the problems of obstetrics and gynaecology through the ages.

The book commences with a historical introduction. The author proceeds

to deal with the available knowledge of these problems as derived from the palaeolithic drawings and statuettes. Methods employed by the Red Indians and nations inhabiting vast Siberian provinces are discussed, and a general review of their irrational therapy is outlined, with special attention to the full status of women in those days.

The author goes on to discuss the routine of life in ancient Babylon, Assyria, Persia, and among the ancient Jews in the near East. The significance of hieroglyphics is also discussed. The book contains some interesting information on the obstetric chair as used in ancient and modern Egypt, and the author proceeds to discuss the hygienic views of these nations.

The next section of the book deals with Eastern culture, concerning chiefly China, Japan, and ancient India. In this section, as we find through the whole book, there is an extraordinarily fine set of references to the works on these countries. Here the author gives in some detail their views on the treatment of retained placenta, and a description is given of Caesarean section as practised in old Japan. This is followed by a most complete account of the culture and knowledge of female ailments in ancient Greece and Rome from the earliest times to 400 B.C. The views of Plato and Aristotle are discussed at some length, including the knowledge at that time of female anatomy, physiology, puberty, menstruation, and the menopause, procreation, and development. This is followed by a description of the Roman and Greek lying-in chamber, and the positions adopted during delivery. The Spartan methods are also mentioned.

Considerable attention is given to a description of the care of the newborn, particularly in ancient Rome. This includes a description and drawings of primitive varieties of feeding-bottles and, in addition, reviews the knowledge of the pathology of gynaecological symptoms, including such things as the anomalies of the periods, e.g. amenorrhoea and oligomenorrhoea. Attention is drawn to the first account in the literature of retention of the menses.

Sterility is thoroughly reviewed and abortion is discussed at some length. The pathological conditions of the breast which occur in conjunction with pregnancy and the puerperium are mentioned and the ancient methods of treatment outlined, including massage and hydrotherapy. Methods of preventing pain and of securing haemostasis and various gynaecological and obstetric operations are discussed. Female hygiene, dress, the hygiene of sex, of the puerperium, and the position of women in the community are also discussed.

This book is full of a wealth of anthropological knowledge which is of considerable interest to the gynaecologist and obstetrician; in fact, we could say that this is the best book written in modern years on the history of our subject.

The effect of various religions upon sex life in general is discussed in different portions of the book, and the particular effects of the introduction of Christianity upon the status of woman is mentioned at some length. We feel that the author has produced a work which is definitely worthy of him, not only from the point of view of the material which he has given us, but also from his enormous number of references in the bibliography, which indicate profound researches into the literature.

Barton Gilbert.

"Maternal Deaths. The Ways to Prevention," by IAGO GALDSTON, M.D. The Commonwealth Fund.

This monograph sets out in a clear and attractive manner, both to the medical profession and to the educated lay public, the reasons for the 1,343 preventable deaths in childbirth which occurred in 1930 and 1932 in New York City, and suggests methods by which the maternity service might be improved.

The author rightly stresses the importance of the education of the public in all matters concerned with health, and especially with the health and proper care of the pregnant woman. Much yet remains to be done in the way of training women to demand and to expect the very best treatment during this time, and in order to eradicate by education the non-co-operative patient, whose refusal to co-operate is, in so many cases, due either to ignorance or to economic difficulties.

A brief résumé is given of antepartum care from the point of view of both patient and physician, and there are interesting chapters on the technique of the attendant in labour and the place of the midwife in obstetric practice. Many failures in aseptic technique are recorded which have resulted in puerperal fever, and the author would not tolerate the control of deliveries by midwives if it were economically possible to do without them.

The argument of *home versus hospital confinement* is discussed with clarity and fairness, with a bias towards confinement in hospital if this is in a recognized institution.

There is an excellent and sanely written chapter on the dangers of unnecessary operative interference, and on anaesthetics and analgesics in labour; finally, good suggestions are made as to what can be done by the medical profession, health departments, and the public in general to reduce maternal mortality. In an appendix an interesting description is given of methods used by the Cleveland Hospital Obstetric Society, Cleveland, Ohio; and of the good results which they have obtained.

This small book, despite a certain tendency to repetition, should be valuable, especially if put within the reach of the lay public. It is attractively produced and well printed.

M.S.

"Leucoplasia de la Vulva. Leucoplasia pura y complicada con Kraurosis," by DR. PEDRO FIGUEROA CASAS. Libreria y Editorial Ruiz Rosario, 1937.

This excellent little book gives a comprehensive account of leucoplakia and kraurosis vulvae, beginning with a historical survey.

The author's observations are based upon a series of 20 cases occurring in 10 years in the gynaecological service of the Espanol and Centanario Hospitals.

Aetiological factors are discussed at length, stress being laid upon the frequency with which ovarian insufficiency in varying degrees is found in patients with these lesions and their possible association with psychogenic factors, which is being more fully investigated at the moment.

The pathogenesis is not yet fully understood, but full accounts are given of the neurotrophic, and the inflammatory theories of origin of the recent theory that the condition may be caused by lack of vitamin A, is discussed, though adequate proof of this is, as yet, lacking. A clear description is given of the signs, symptoms and course of the disease, and the differential diagnosis is discussed at length. There is an excellent chapter on the pathology of the condition.

Clinical records of the author's cases are given, and there are many good photographs and microphotographs.

The difficult problem of the treatment is discussed in detail, and in the early stages intensive treatment by hormones is recommended; surgical treatment may be graded according to the severity of the lesion, beginning with resection of the internal pudendal nerves, presacral sympathectomy, and, in advanced cases, excision of the vulva. It is recommended that the latter operation should be followed by hormone therapy in order to avoid recurrences in the scar.

In this book the author gives a comprehensive, but compact and well-arranged account of these most interesting diseases, and the publication can be heartily recommended.

M.S.

"Insufflation Tubaire Kymographique par la Méthode de Rubin," by Louis Bonnet. G. Doin & Co.

M. Bonnet's short monograph gives in the concise and lucid manner, which is characteristic of the French nation, an admirable account of tubal insufflation by Rubin's method, using a kymograph to register the variations of intratubal pressure which are shown by the rythmic contractions of the Fallopian tubes.

A historical survey is followed by a description of the principles of the method and of Rubin's apparatus and the author's modification of it.

Tracings are given, showing the type of contraction obtained in permeable and impermeable Fallopian tubes, tubal spasm and tubal stenosis. A section is devoted to localization of obstruction in the Fallopian tubes of auscultation, situation of pain experienced by the patient, and by radiography. A study of the oscillations obtained in tracings will give information as to the state of the Fallopian tubes and, as the author suggests in an interesting chapter, may also help in the evaluation of the ovarian function of the patient.

A summary of results is given and a concise description of contra-indications and complications of the operation.

This method compares favourably with dilatation and insufflation alone and with the results obtained from lipiodol examinations; it should, in the opinion of the author, be performed in preference to the lipiodol method unless an obstruction is diagnosed, when the kymographic method should be followed by radiological examination after the injection of lipiodol.

M.S.

Review of Current Literature.

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab), F.R.C.S., F.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the following journals with which the "Journal of Obstetrics and Gynæcology of the British Empire" exchanges :—

British.—The Lancet; British Medical Journal.

Canadian.—The Canadian Medical Association Journal; Bulletin Médical de Quebec.

Australian.—Medical Journal of Australia; The Australian and New Zealand Journal of Surgery.

Indian.—The Calcutta Medical Journal.

American.—American Journal of Obstetrics and Gynecology; The Journal of the American Medical Association; Surgery, Gynecology and Obstetrics; American Journal of Diseases of Children.

French.—La Gynécologie; Gynécologie et Obstétrique; Bulletin de la Société d'Obstétrique et de Gynécologie de Paris.

Belgian.—Bruxelles Médical.

Italian.—Annali di Obstetrica e Ginecologia; Archivo di Obstetrica e Ginecologia; Revista Italiana di Ginecologia, Bologna.

German.—Archiv für Gynäkologie; Zeitschrift für Geburtshülfe und Gynäkologie; Zentralblatt für Gynäkologie; Monatsschrift für Geburtshülfe und Gynäkologie; Münchener Medizinsche Wochenschrift; Monatsschrift für Krebsbekampfung.

Scandinavian.—Acta Obstetrica Scandinavica.

South American.—Boletin de la Sociedad Obstetricia y Ginecologia de Buenos Ayres.

Japanese.—Japanese Journal of Obstetrics and Gynæcology.

The Review of Current Literature thus keeps the readers of the Journal in touch with current literature throughout the world. At the end of the year an Index of all the subjects contained in the articles of the above journals is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology and Biochemistry.

LIST OF ABSTRACTORS.

London: J. BEATTIE, F.R.C.S.; A. C. BELL, F.R.C.S.; R. K. BOWES, F.R.C.S.; J. LYLE CAMERON, F.R.C.S.; ALBERT DAVIS, F.R.C.S.; F. H. FINLAISON, F.R.C.S.; B. GILBERT, F.R.C.S.; R. J. KELLAR, F.R.C.S.; R. LIGHTWOOD, F.R.C.P.; J. A. MOORE, F.R.C.S.; C. D. READ, F.R.C.S. (Edin.); F. ROQUES, F.R.C.S.; R. WINTERTON, F.R.C.S.

Felsted: W. E. CROWTHER, M.B.

Leeds: R. H. B. ADAMSON, M.D., AND B. JEAFFRESON, F.R.C.S.

Liverpool: M. DATNOW, F.R.C.S.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.

Manchester: R. NEWTON, M.D.

Glasgow: JANE H. FILSHILL.

The Lancet.

Vol. ccxxxii, No. 5,914, January 2nd, 1937.
*Incidence of anaemia in pregnancy. W. J. S. Reid and Jean W. Mackintosh.

Vol. ccxxxii, No. 5,925, March 20th, 1937.
*Heart disease with normal rhythm complicating pregnancy. Kenneth Harris.

Vol. ccxxxii, No. 5,937, June 12th, 1937.
*Effect of calcium and vitamins A and D on the incidence of pregnancy toxaemia. G. W. Theobald.

Vol. ccxxxii, No. 5,939, June 26th, 1937.
*Menstrual fistulae. Glyn Maliphant.

Vol. ccxxxii, No. 5,951, September 18th, 1937.
*Inhibition of menstruation and ovulation by means of testosterone propionate. S. Zuckerman.
*A case of severe toxic jaundice in late pregnancy with recovery. Mary Fraser.

Vol. ccxxxii, No. 5,954, October 9th, 1937.
*Absorption and excretion of oestrone by the human organism. Tage Kemp.

Vol. ccxxxii, No. 5,961, November 27th, 1937.
*Treatment of 106 cases of puerperal fever by sulphanilamide. Leonard Colebrook and Anthony W. Purdie.

Vol. ccxxxiii, No. 5,963, December 11th, 1937.
*The influence of anaemia and poor social circumstances during pregnancy. W. J. S. Reid and Jean Mackintosh.

Incidence of Anaemia in Pregnancy.

The incidence of anaemia in pregnancy has been much disputed. Davidson found the percentage of haemoglobin was below 70 in 17.5 per cent of 800 pregnant women. Mackay found the figure was 4.6 per cent in 109 cases, Boycott 11 per cent in 222, and Moore, Lyon, Galloway and others anything from 20 to 80 per cent. In their very exhaustive investigation of over 1,000 women Reed and Mackintosh obtained the figure of 10.2 per cent. In all their cases the anaemia was hypochromic. The incidence of anaemia varied directly with the economic position of the patients, but multiparity did not appear to have much influence, nor did age, work or type of pregnancy.

Heart Disease with Normal Rhythm Complicating Pregnancy.

This paper is a description of 100 cases of heart disease complicating pregnancy, and it stresses what most obstetricians have long observed clinically, namely, that it is the functional state of the heart rather than any anatomical lesion which is the important factor.

Of these cases 81 had mitral stenosis alone, 13 had mitral stenosis and aortic regurgitation, and 6 aortic regurgitation alone. No difference was found in prognosis between any of these lesions, but the size of the heart appears to be important from this point of view, the death-rate being definitely higher when the heart was enlarged. Eighteen patients developed congestive heart failure during the course of pregnancy. Although none of them died during pregnancy or labour, 22 per cent died later, in contrast to the 12 per cent mortality of those who had not had congestive failure. This mortality was higher when the failure occurred during the first pregnancy than in multiparae. From these results the author concludes that a careful investigation into the histories of the patients' exercise-tolerance before and during pregnancy is of paramount importance for it is upon this that the conduct of the case depends. Congestive heart failure is a very serious incident, and pregnancy is contra-indicated in those cases which give such a history. It should be treated as soon as possible by evacuation of the uterus as soon as the failure has been relieved by rest and other medical measures.

EFFECT OF CALCIUM AND VITAMINS A AND D ON INCIDENCE OF PREGNANCY TOXAEMIA.

In an endeavour to ascertain whether calcium and vitamins A and D had any effect on the incidence of pregnancy toxaemia, the present investigation on 50 women attending antenatal clinics was carried out, 50 similar women being used as a control. From the results it would appear that toxic symptoms were definitely more common in the untreated patients.

It is a little unfortunate that three such dissimilar substances as calcium, vitamin A and vitamin D should have been used as a basis for this research, for it is naturally impossible to assess the relative value of each. The results, however, are interesting and more than justify further experiment.

MENSTRUAL FISTULAE.

Utero-parietal fistulae must be very uncommon, and it is surprising that as many as 70 cases have been recorded. In the present case the aetiology was a tuberculous abscess with drainage, and blood escaped copiously from the abdominal end of the sinus with each menstruation. It appears that spontaneous closure is very unusual, but the author apparently obtained a permanent cure by excision.

INHIBITION OF MENSTRUATION AND OVULATION BY MEANS OF TESTOSTRONE PROPIONATE.

It is well known that the administration of anterior pituitary substance, of progestin and of oestrogenic substances can inhibit oestrus. These hormones appear to be similarly effectve in the course of the menstrual cycle, for they can inhibit bleeding both in monkeys and in women. The author has produced the same results from the administration of testostrone propionate to monkeys. The internal reproductive organs are not injured by the treatment, but follicular growth and luteinization are both inhibited, and he suggests that this substance may be of clinical value in the control of uterine bleeding in the human. This suggestion has recently been applied

by Loeser (personal communication) with considerable success in the induction of temporary sterility and for menorrhagia.

A Case of Severe Toxic Jaundice in Late Pregnancy with Recovery.

A case is reported of extremely severe toxic jaundice with pregnancy. Unlike the majority of such cases the patient recovered after the induction of premature labour and the administration of intravenous glucose saline. Catarrhal jaundice is by no means an infrequent complication of pregnancy, but in the great majority of cases neither mother nor child suffer any serious disability. There is, however, apparently very little connexion between the two conditions, and transition from one to the other is unusual.

Absorption and Excretion of Oestrone by the Human Organism.

The enormous popularity of hormone therapy in gynaecology has far outstripped the more detailed knowledge of its uses, and though experimental work is being carried out with great rapidity very little attention has been devoted to the actual fate of this substance in the body. To remedy this Kemp and Pedersen-Bjergaard have investigated the absorption and excretion of oestrin in the human. They find that from 3 per cent to 12 per cent is excreted in the urine shortly after administration. The proportion is greater after oral than after parenteral administration, and that in the former case the quantity excreted is proportionate to the dose administered. It is also very rapidly absorbed and excreted by the body and has therefore a low specific biological action. The authors consequently recommend that oestrin should be given in such a form that it can be absorbed slowly, the dosage being spread over comparatively short intervals.

Treatment of 106 Cases of Puerperal Fever by Sulphanilamide.

This paper embodies the results of the treatment of over 100 cases of puerperal fever by sulphanilamide at Queen Charlotte's Hospital. The results are summarized as follows. (1) Of the 106 cases of puerperal sepsis treated by sulphanilamide, usually given by the mouth alone, 100 were infected by haemolytic streptococci, 3 were infected by anaerobic streptococci, and three by staphylococci. (2) The clinical courses of the 100 cases infected by haemolytic streptococci have been on the whole similar to those of the 64 cases previously treated by sulphamido-chrysoidine. The average stay in hospital was 19.7 days as compared with 31.3 days in 1935. (3) There were 8 deaths among the 100 cases but only three of them can be regarded as deaths from straightforward sepsis in patients who lived long enough for chemotherapy to have a fair trial. The mortality-rate for all cases, 199, infected by haemolytic streptococci since the beginning of 1936, when treatment by sulphamido-chrysoidine and prontosil soluble was begun, has been 5.5 per cent as compared with the average of 22.8 per cent for the preceding five years. (4) Drug fever was suspected in several instances. (5) Some degree of cyanosis developed in 58 cases and was usually associated with methaemoglobinaemia and sulph-haemoglobinaemia. (6) Other toxic manifestations of the drug observed much less frequently have included prostration, paraesthesia, headache, visual disturbances, and joint pains. No generalized rashes developed.

THE INFLUENCE OF ANAEMIA AND POOR SOCIAL CIRCUMSTANCES DURING PREGNANCY.

Further to their original paper on the incidence of anaemia in pregnancy, Reid and Mackintosh have made an attempt to estimate its influence on the subsequent history of mother and child. They found that the incidence of toxaemia of pregnancy did not appear to be influenced by the anaemia, nor did it have any influence in producing any abnormalities in labour. The duration of labour and the birth of the child were similarly unaffected, but both the neonatal death-rate and the infantile death-rate were definitely higher.

Albert Davis.

British Medical Journal.

No. 4,007, October 23rd, 1937.

*Puerperal infection in relation to midwifery attendants. J. L. Miller Wood.

PUERPERAL INFECTION IN RELATION TO MIDWIFERY ATTENDANTS.

This paper discusses at length the vexed question of puerperal sepsis in relation to the midwifery attendant. It is gratifying to note that the writers do not recommend routine swabbing of throats of everyone who practises midwifery, for it is well known that the results obtained are usually confusing and generally inaccurate. In the reviewer's own hospital the percentage of positive swabs was so high in a recent wholesale investigation that if all the infected midwives had been suspended the department would have had to have been closed. The authors conclude that not only is it essential that all cases of pyrexia during the puerperium should be carefully investigated as a routine, but that the presence of the streptococcus pyogenes in the throat in any of the attendants preclude him or her from midwifery practice until the swab is negative. The swabbing of clinically normal throats, unless they are believed to be a source of infection, cannot be too strongly deprecated.

Albert Davis.

The Canadian Medical Association Journal.

Vol. xxxvii, No. 5, November 1937.

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JOURNAL OF OBSTETRICS AND GYNAECOLOGY

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THE PHYSICAL WELFARE OF THE DIONNE QUINTUPLETS.

A report is presented dealing with the physical welfare of the quintuplets during the first three years of life. Their home, a newly built and elaborately planned structure, near the abode of their birth, stands on a small estate, powerfully fenced against any ingression. On one side is a building separated by glass and a fine wire screen, where visitors may see the children in their playground. Trees have been planted, the grounds have been laid out, and means provided to attract birds in the summer and feed them in winter. The electric supply for lighting and heating and running the estate and adjoining farm is brought in by power lines, and a sixty-foot drilled well supplies water. Sewage is carried to a septic tank and from there to a well-tilled field.

The permanent staff of the children's home consists of nine members: two nurses, one teacher, three policemen, a housekeeper and two maids, further help being added when necessary during the summer to supervise the numerous visitors. The policemen are on duty day and night to guard the children and control observers. The nurses are responsible for the care and training of the children and the keeping of records.

These children, by special Act of the Parliament of Ontario, are under the control of the Crown, assisted by a group of specially appointed guardians who meet monthly, having control of all business affairs and other matters pertaining to the children's estate. The guardians serve without a salary, but employ a business manager, secretary-treasurer, legal adviser and auditor of accounts. The income accruing to the children is derived from contracts for motion and still pictures and from endorsement of products utilized by them, subject to the approval of Dr. Dafoe, their medical adviser, and the guardians. Half a million dollars, including the property value of their estate, 60,000 dollars, represents their financial holding. The capital, invested in government securities, provides the income used to meet the expenses which amount to about 1,800 dollars a month.

Regularity has been an outstanding principle followed in the general care of the children. For the first year and a half 18 hours of sleep a day were obtained, afterwards this was reduced to 12 hours at night and 1½ hours in the afternoon. They receive orange juice, then breakfast, which is followed by a play period, when they are allowed all possible freedom. Before lunch they have music, songs and group play for 15 minutes, followed by a short rest on mats. After mid-day lunch they sleep and again play in the open. They are bathed before supper, which is served at 6 p.m. after which they are undressed and short stories are read to them. Then they say their prayers and are put to bed.

Elaborate wardrobes, with equipment for all changes of weather and temperature, are provided. Cotton garments are worn next to the skin, and woollen clothing is added as the weather becomes colder. The children are encouraged to dress themselves as far as possible and to put away their

own clothing. One nurse takes her meals with the children and instructs them in good table manners, and a strict routine during meals is followed.

Their physical development appears to have progressed rapidly in spite of their prematurity at birth. There has been a steady increase in weight, and an almost total absence of gastro-intestinal disorder; their appetites have been good, and a minimum of persuasion to eat has been employed. The greatest care has been taken to protect the children from infections, by isolating them from the public, and by the wearing of masks and gowns by the attendants. In spite of these precautions, some upper respiratory infections occurred. They were all given, as a special prophylactic measure, three diphtheria toxoid injections at three weeks' interval when one and a half years old. No reactions followed. They were vaccinated against smallpox. Examinations have been carried out showing good general development, bodily and mentally. Their special senses appear to be normal.

Some astigmatism was found in one of the children, and in another poor co-ordination of the eye muscles, but these defects are very slight.

This article includes charts giving their diet and times and methods of feeding for the first three years, also pictures of dental casts, charts of illness and infection and two photographs of the children at six months and at three years and five months, respectively.

ABSTRACTS OF STUDIES ON THE DEVELOPMENT OF THE DIONNE QUINTUPLETS.

The author holds the view that these children are monozygotic quintuplets, derived from a single ovum, as there was only one chorion, there is a most remarkable similarity in all hereditary characteristics and there is no evidence of twins in the family for three generations. Charts are given showing similarity of characteristics in blood group, iris colour, iris pattern, eye refraction errors, eyelashes, eyebrows, hair colour, hair form, hair whorl, skin colour. The only differences noted are a slight variation in eye refraction error and a reversed hair whorl exhibited by one of the children. Finger patterns also reveal an outstanding similarity.

Intelligence tests were administered every two weeks. All fall short of the normal for their chronological age. This was probably due to their prematurity at birth, and as they were a social group from birth, communication for social intercourse was probably retarded, as is usually the case with twins. Motor tests showed a normal level, personal, social and language tests were also well up to normal or even above it. The results from all these tests appeared to be of a higher order with increasing age. The children appear to respond well to routine training, especially in self-discipline. There appeared, however, to be a slight retardation in language development, and it was apparent to the author that these children made use of gesture and pantomime to convey their desires to each other and to adults.

Numerous charts and diagrams are given to illustrate characteristics, mental development, results of mental tests and daily routine activities, as well as progress in pronouncing syllables.

ATROPHIC RHINITIS: THE CONSTITUTIONAL FACTOR: THE TREATMENT WITH OESTROGENIC HORMONES.

A study has been made of the X-ray photographs of 68 cases of atrophic

rhinitis and ozoena and the evidence deduced leads one to believe that in a large majority there was a dyspituitary state during, ar after, the growth period. It has been suggested that the disease has been produced by the mating of dyspituitary individuals in whom anterior lobe function is unstable in secretory activity, nature or time of activity, and the condition occurs as a genetically transmitted, varyingly localized, focus in a special familial constitution. Theoretical speculation upon the process by which a dyspituitary constitution might affect the morphologically specialized mucosa of the turbinate bones, led the authors to investigate the naso-genital relation in the monkey and to recognize the fact that the administration of oestrogenic substances is followed by specific responses in the said turbinal mucosa, very closely resembling that occurring in other sex-skin areas as was previously reported. These specific changes appeared to be of an order opposed to the pathological changes occurring in atrophic rhinitis and this led the authors to make a trial application of dihydroxyoestrin locally to the nose when this disease was manifest.

Thirty-one female and seven male patients suffering from ozoena and atrophic rhinitis were treated with insufflations of oestrogenic hormone. The results led the authors to believe that this treatment was very much more effective than any other at present available. Seven additional cases suffering from atrophic rhinitis together with progressive deafness, and one case which showed in addition to those two affections considerable otosclerosis, were similarly treated.

Numerous tables and charts are included in the text, illustrating types of cases, dosages, conditions and the results of treatment.

Pentothal Sodium as a Hypnotic in Obstetrics.

The authors have made a study of the administration of pentothal sodium to 238 women in labour without any noticeable harmful effects to the mother or child. It appeared that, unlike ordinary barbiturates, this thio-derivative did not cause excitement at any time. Furthermore, the hypnotic action of pentothal sodium appeared to be attended by a marked degree of amnesia. One of the conclusions reached was that labour was shortened in duration. The method of administration was to give capsules by mouth, 4 grains being allowed as soon as pains were definitely established, 3 grains being repeated half an hour later, and again at the end of one hour. If required, 2 to 3 grains might be repeated every half hour to one hour if the effects seemed to be wearing off.

Scopolamine, 1/100 to 1/150 grain, was given at the time of the first dose. Pentothal sodium may also be given in solution *per rectum*. The dose used was 7½ grains dissolved in 25 c.c. of water and repeated in an hour's time. A further series of 120 additional obstetrical cases were treated as mentioned and the results were stated to be quite satisfactory.

A full bibliography is appended.

Neonatal Mortality.

The causes of stillbirths and neonatal deaths are still extremely obscure. Between the years 1926 to 1936 there were 6,954 births considered by the author, and out of these there were 453 neonatal deaths, or 6.51 per cent.

A table inserted reveals that many of these deaths were listed under such indeterminate names as stillbirth (155), prematurity (146), inanition (24), difficult labour (15), atelectasis (7), and convulsions (6). The author is of the opinion that these terms in no way reveal the cause, and should never be employed. A table is included showing the number of cases attended by different medical men and their mortality rates. There is a lower mortality rate in the practice of medical men who attend many confinements, and the inference is advanced that skill and experience have played a beneficial part. It is further pointed out that among the families of doctors there were no neonatal deaths, the inference again being drawn that care and attention have been rewarded.

Quoting from the same series, there were 42 cases of Caesarean section, or one in 166 cases, with a maternal mortality rate of 4.76 as compared with a general mortality of 0.6 per cent. The author, however, is of the opinion that a properly timed Caesarean section entails less risk for the mother than craniotomy, and, of course, the neonatal death-rate is definitely diminished. The author urges greater antenatal care, including Wassermann tests in all cases, improved resuscitative methods for the newborn and the provision of efficient equipment for the care of premature infants.

PRE-NATAL AND POST-NATAL CARE.

In the province of Nova Scotia, the maternal mortality rate is about 0.5 per cent. At the hospital under the author's care the death-rate is about 0.25 per cent; expert antenatal observation and care during labour share the credit. Details of antenatal care are given, which include investigation of bodily conditions, focal sepsis, Wassermann tests, estimation of weight increase, blood-pressure, urine examination, X-ray examination, presentation, position, and cephalo-pelvic proportions. Careful watch is kept for toxaemias which are treated by rest, diet and elimination, and when there is no definite improvement, by termination of the pregnancy. Abortions are treated with the same care as labours, septic cases being treated expectantly. Haemorrhages, either in cases of abortion or post-partum, are regarded as strongly predisposing to infection. Such complications as diabetes, organic heart disease or tuberculosis having a higher death-rate among pregnant than non-pregnant women, require special regard and treatment.

Post-partum care takes into consideration such conditions as uterine retroversion, which is regarded as unimportant, prolapse, which should be corrected by a plastic operation, or, if slight, by a ring pessary. Contraceptive measures are advocated when it is considered wise to delay pregnancy for a year or more, as in cases of severe lacerations, or prolapse requiring repair, or when it might be inadvisable for the patient again to conceive, as when renal damage has followed severe toxaemia.

STERILITY.

Involuntary sterility affects three million couples in the United States and 140,000 in Canada. The male is responsible for 33 per cent of cases, and a complete investigation of the male should be made before the female is subjected to any treatment. Investigation of the female requires a com-

plete general and pelvic examination. General examination entails metabolic tests; local examination takes into consideration the development of the uterus and the patency of the Fallopian tubes. In the treatment of sterility a few special surgical measures are considered, such as epidydimovasostomy in the male, and the operations of salpingostomy, tubal implantation and ovarian implantation in the female. Hormone therapy is also discussed, and the fertility period is also considered. The author is of the opinion that no case should be denied the benefits which frequently accrue from careful investigation and judicious treatment.

J. Lyle Cameron.

The Journal of the American Medical Association

Vol. cix, No. 19, November 6th, 1937.

Mode of action of sulphanilamide. Eleanor A. Bliss and P. H. Long.

Vol. cix, No. 20, November 13th, 1937.

*Breech delivery. M. P. Urnes and H. J. Timerman.

Syncytial reaction of pregnancy. R. M. Choisser and B. Notes.

The use and abuse of ergot and pituitrin. Special article.

Vol. cix, No. 21, November 20th, 1937.

Ovarian fibroma with ascites and hydrothorax. J. E. Rhoads and A. W. Terrell.

Uterine myomata. Virgil S. Counseller.

Vol. cix, No. 22, November 27th, 1937.

Theelin therapy in psychoses. E. F. Hoctor and A. A. Werner.

Unusual relation between menstrual function and ascites. S. W. Hartwell and W. R. Johnson.

Vol. cix, No. 23, December 4th, 1937.

*Amenorrhoea. R. T. Frank, M. A. Goldberger, U. J. Salmon, and Gertrude Felshin.

Menorrhagia and metrorrhagia. J. C. Burch, G. S. McClellan, J. W. Simpson, C. D. Johnson, and E. T. Ellison.

Sterility and abortion. J. C. Litzenberg.

*Endocrine treatment of vaginitis. R. M. Lewis and Eleanor L. Adler.

Endocrine treatment of menopausal phenomena. J. P. Pratt and W. L. Thomas.

BREECH DELIVERY.

This paper deals with 346 breech presentations delivered at the Chicago Maternity Centre, nearly 80 per cent of the mothers being multiparae. The main purpose of the article is to deal with the most suitable form of anaesthesia for these cases, the obstetric treatment being expectant in multiparae, and routine episiotomy with application of forceps to the aftercoming head in primiparae.

Pudendal block anaesthesia with one per cent of procaine hydrochloride is suggested as the ideal for the uncomplicated cases, for episiotomy and low forceps; it can be employed without further anaesthesia, the co-operation of the patient is retained, and stretching of the perineum is painless. The authors describe their technique of pudental block anaesthesia, which they admit does not give uterine relaxation sufficient for breech extraction, and, if this proves necessary, presacral block anaesthesia is induced. In some cases uterine relaxation may still be deficient; ether was also employed in those.

The authors believe that a great advantage of local anaesthesia is that it dispenses with the services of a skilled anaesthetist without added risk to mother or child.

There was one maternal death in the series, due to miliary tuberculosis. Sixty-five foetûs were stillborn, but when non-viable foetûs, or macerated foetûs and monsters were deducted, the corrected foetal mortality was 6.6 per cent, which, it is claimed, compares favourably with results published from other hospitals.

AMENORRHOEA.

The 27 patients in this series included six cases of primary amenorrhoea. Routine examination included tests of basal metabolism, sugar tolerance, blood examination, X-ray films of the sella turcica and pelvic examination. All patients proved normal to these tests, but three had hirsuties and two of these also had enlarged clitorides.

In 21 cases complete oestrogenic examination of the urine over a period of a month was made, and the patients were found to fall into four groups, according to the total amount of oestrogenic substance excreted in the urine in a month. (1) *Low* (50 to 200 mouse-units): 7 cases, 3 of them cases of primary amenorrhoea. (2) *Subthreshold* (500 to 850 mouse-units): 5 cases, 2 being primary. (3) *Normal* (1,000 to 1,714 mouse-units): 6 cases, 1 being primary. (4) *Excessive* (2,075 to 2,328 mouse-units): 3 cases, 1 being primary.

Gonadotropic studies of the blood and urine were carried out in 10 cases. Four of these, all cases of secondary amenorrhoea, showed continuous and persistently high gonadotropic secretion. Curiously enough these cases fell into 1 of each of the 4 oestrogenic groups described. In 6 other cases, 4 of which were primary and 2 secondary, gonadotropic secretion was absent. Again each of the 4 oestrogenic groups was represented.

The administration of oestrogenic substances to the patients in this series gave disappointing results, in distinction to the results in menopausal conditions, which almost invariably respond to such treatment. It was also found that enormous and continuous doses of oestrogens were necessary to diminish excessive gonadotropic secretion in this series, whereas at the menopause gonadotropic oversecretion rapidly abates with the administration of oestrogens.

In no case treated did menstruation persist after the cessation of treatment, and the authors now advise the abandonment of oestrogens in the treatment of amenorrhoea.

Treatment with gonadotropic substances, though more rational, proved equally ineffective in curing any case of amenorrhoea, and so no evidence

pointing towards a primary pituitary, or primary ovarian, cause of amenorrhoea could be demonstrated, but the authors suggest that the use of gonadotropic substances in higher doses than employed by them is worthy of further trial.

This paper, then, fails to find the cause or causes of amenorrhoea, but the authors suggest that a failure on the part of the uterus to respond to endocrines must be considered in the aetiology.

ENDOCRINE TREATMENT OF VAGINITIS OF CHILDREN, AND OF WOMEN AFTER THE MENOPAUSE.

The administration of oestrogenic substance to the child changes the thin vaginal mucosa to one resembling the thick epidermis-like structure of the adult. This change is temporary, and reversion to normal occurs on withdrawing the oestrogen. It has also been shown that oestrogenic substances cause, in the child, a strongly acid vaginal secretion, as in a normally menstruating woman.

Before puberty and after the menopause the vaginal mucosa is a thin delicate structure with a so-called secretion which is faintly acid or neutral in reaction, and is readily susceptible to infection.

Knowledge of these facts has been used in the treatment of gonococcal vaginitis in children with oestrogenic substances alone. The methods of administration have varied. Hypodermic injections of oestrogenic substances are sometimes followed by enlargement of the breasts, and slight menstrual discharges, and the authors at present employ vaginal suppositories. The substance used by them is amniotin, the dosage being about 500 international units in a gelatine capsule. This may be inserted nightly by the child's mother, and no other treatment is required beyond preliminary cleaning of the vulva when necessary.

On the average smears became negative in 24 days, but it is probably wise to continue treatment for eight weeks. Using this method no unpleasant side effects occurred, and 80 out of 82 patients were cured. A few apparently relapsed, but the authors believe that this was due to re-infection, and noted that a second course of treatment resulted in a more rapid cure. In such cases careful examination of the cervix, rectum, and urethra should be made.

Post-menopausal vaginitis was successfully treated by the hypodermic injection of 500 international units of oestrogenic substance three times weekly for six weeks No relief was obtained in cases of leucoplakia vulvae.

F. H. Finlaison.

New York State Journal of Medicine

Vol. xxxvi, No. 22, November 15th, 1937.

*Analgesia and anaesthesia in obstetrics, pentothal sodium, cyclopropane, and vinyl ether. W. Bourne.

ANALGESIA AND ANAESTHESIA IN OBSTETRICS, PENTOTHAL SODIUM, CYCLOPROPANE AND VINYL ETHER.

Following the work of MacPhail, Gray, and Bourne on the use of pento-

thal sodium as a hypnotic in labour, Bourne has reported on the use of nitrous oxide, cyclopropane, and vinyl ether for analgesia or anaesthesia to follow the administration of pentothal.

If nitrous oxide is given intermittently from an early stage, care being taken to avoid anoxemia, no harmful effects are found, even after prolonged administrations. In the case of cyclopropane such a high percentage of oxygen may be given that anoxaemia is out of the question. Moreover cyclopropane does not cause retention of dye in hepatic function tests. Cyclopropane is also recommended for the operation of Caesarean section. At the same time a warning is given against the self-administration of these gases from fool-proof machines.

These gases both require expert administrations, so for the general practitioner the use of vinyl ether is recommended. It is very safe for mother and child, it is easy to administer, any desired stage of narcosis being easily maintained, and recovery is rapid and uneventful. When administered by the open method, it is recommended that a mixture containing 25 per cent of vinyl ether and 75 per cent of ethyl ether be used.

G. C. Steele.

Surgery, Gynecology and Obstetrics.

Vol. lxvi, No. 1, January 1938.

*Diabetes and pregnancy. W. W. Herrick and A. J. B. Tillman.

*The upper pelvic floor and its importance in total abdominal hysterectomy. L. K. P. Farrar.

*The interposition operation with sterilization. F. I. Harris.

*Uterus bicornis duplex associated with infection due to micro-aerophilic haemolytic streptococcus. E. B. Self and F. L. Meleney.

Diabetes and Pregnancy.

Herrick and Tillman have made a study of 56 patients with diabetes in 67 pregnancies. A family history of diabetes occurred in 17.8 per cent; a family history of vascular disease was of equally common occurrence. As far as could be ascertained in none of the patients did the disease begin before puberty. In 15 cases the disease began during pregnancy.

The past obstetrical history showed repeated stillbirths, abortions and neonatal deaths. The reproductive capacity of these patients is low, and the incidence of vascular disease and hyperthyroidism is high.

Vomiting of early pregnancy augments the danger of diabetic acidosis, so that a serious ketosis may rapidly develop. In some such cases abortion may occur before coma. For this reason the regulation of diet and insulin in the first trimester may be difficult or impossible. A high carbohydrate intake is best adapted to the treatment of ketosis of diabetes and the vomiting of pregnancy. Herrick and Tillman have made it a general practice to supply 200 grams of carbohydrate daily to the diabetic patient with vomiting of pregnancy, given five or six times at intervals of 2 hours, with insulin as often as is indicated. The next step is the building up of a more normal diet in which the number of calories per kilogram varies inversely with the weight of the patient. In the second trimester there is little change in the

basic requirements of diet and insulin, but between the sixth and ninth month marked changes in tolerance are to be expected, and these vary in degree and in time of appearance with the individual patient. Decline in tolerance if not promptly treated, may result in destruction of the foetus.

Labour in the diabetic patient is critical. Anaesthesia tends to induce coma. In the authors' cases the hazard of infection was as pronounced as in cases reported elsewhere. There was a puerperal morbidity of 41 per cent. Out of the 67 cases delivered 25 were spontaneous deliveries, 16 instrumental, and 8 were delivered by Caesarean section. There were 10 cases of dilatation and curettage, 4 of hysterotomy and sterilization, and 5 spontaneous abortions. In none of the cases of Caesarean section was this mode of delivery undertaken because of diabetes alone, and the authors, since they had no maternal deaths during pregnancy, the puerperium or the follow-up, feel that they cannot find any strong argument for radical methods of delivery in this disease, at least from the standpoint of maternal security. On the side of the foetus Caesarean section is a more debatable matter. Caesarean section is performed shortly after viability to save the child, but it should be remembered that every baby thus delivered is premature, and in a review of 300 cases of prematurity Wilcox reports a mortality of 25 per cent regardless of the method of delivery.

The authors have come to the conclusion that the routine performance of Caesarean section in uncomplicated maternal diabetes is unwise. The foetal mortality in this study was 28.3 per cent—this included 4 spontaneous abortions in 9 inadequately treated diabetic mothers and 4 with serious complications such as Bandl's ring, prolapsed cord and large fibromyomata. Excluding cases of this kind the corrected mortality is 3.7 per cent.

THE UPPER PELVIC FLOOR AND ITS IMPORTANCE IN TOTAL ABDOMINAL HYSTERECTOMY.

The upper pelvic floor is made of the unstriped muscle, elastic and connective tissue derived from, or attached to, the lower part of the uterus and vagina. It includes the fibrous bands or sheaths of the nerves, blood-vessels, lymphatics and ureters lying in the broad ligaments, the levator ani muscles and their fascial coverings which are attached to that of the compressor urethrae anteriorly, to the ischial spines and to the coccyx posteriorly and which blend with the aponeurosis of the muscles which lie above it in the broad ligament. In total abdominal hysterectomy it is important to employ a technique by which one may remove the entire uterus without invasion of the broad ligament.

Haemorrhage from the vaginal venous plexus may be avoided by ligating the uterine artery, not only where it enters the uterus, but also before the vaginal and cervical branches are given off from the uterine artery.

Injury to the sympathetic ganglia lying on the posterior leaf of the broad ligament may be avoided by cutting down the broad ligaments close to the sides of the uterus without applying any clamp to the broad ligaments.

By cutting the uterosacral muscles and entering the vagina posteriorly, the uterus will be loosened. A finger introduced into the vagina acts as a guide for the application of clamps to the vagina, ensuring the cutting out of the uterus but eliminating the possibility of cutting too much of the

broad ligament, of injuring the ureters or bladder, of cutting into the uterus and of leaving part of the cervix *in situ*.

Closure of the vaginal wound should be done in an anteroposterior direction. The technique of closure should include (*a*) suture of the muscle walls of the vagina, (*b*) the attaching to them of the round ligaments, uterosacral ligaments, ovarian ligaments if left and the utero-pubic fascial plane, (*c*) the covering of the wound completely and exactly with the vesical peritoneum.

THE INTERPOSITION OPERATION WITH STERILIZATION.

The revival of interest and excellent results recently reported in the treatment of cystocele and prolapse by the operation of interposition, has prompted the author to give a very detailed account of the modern technique of this procedure which has been in use at the Mount Zion Hospital, San Francisco.

The description of the technique is based on an experience with 57 cases, and excellent anatomical and functional results have been obtained in the treatment of cystocele and moderate degrees of prolapse.

It has been used in women during the child-bearing age with the additional procedure of sterilization and has been found to have less morbidity and mortality than laparotomy combined with vaginal plastic procedures in the treatment of this condition.

UTERUS BICORNIS DUPLEX ASSOCIATED WITH INFECTION DUE TO MICRO-AEROPHILIC HAEMOLYTIC STREPTOCOCCUS.

Self and Meleney report a case of uterus bicornis duplex associated with streptococcus haemolyticus. The history of the case is given in detail, and the authors think it important to consider how this organism entered the patient. It may have come through the blood-stream, gaining entrance from the throat, or from the intestine or appendix. However, they think a more likely portal of entry was the anamolous uterus for the following reasons:

(1) The organism is occasionally found in the normal vagina.

(2) Of 16 cases of infection with micro-aerophilic haemolytic streptococcus previously reported by one of the authors, 7 were cases of pelvic infection in women, in whom the uterus and Fallopian tubes were the probable portal of entry. The organism thus appears to have a predilection for the uterus and tubes.

(3) Assuming the organism gained entrance through the vagina, it must have entered the left uterus and either have passed through the opening in the septum to the right side or passed through the left Fallopian tube into the pelvis and thence to the right side.

It is probable that the infection could never have been eradicated in this case (the patient died on the second post-operative day) because of the nature of the congenital anomaly. Any attempt at removal of the infected uterus and tube from above would almost certainly have caused a fatal peritonitis. Drainage from below would have been ineffective.

Sulphanilamide might have had a beneficial effect on the haemolytic streptococcus if used in the early stages, but it would not have had any effect in the later stage.

C. D. Read.

Gynécologie et Obstétrique.

No. 2, August 1937.

REPORT OF THE TENTH FRENCH CONGRESS OF OBSTETRICIANS AND GYNAECOLOGISTS.

First subject for discussion:

1. The treatment of urinary incontinence in women. M. Muret and O. J. Rapin.
2. The treatment of vesico-vaginal fistula. André.

Second subject for discussion:

1. The pathenogenesis of accidental haemorrhage. A. and R. Couvelaire.
2. The treatment of accidental haemorrhage. A. Weymeersch and J. Snoeck.

No. 3, September 1937.

Third subject for discussion:

1. The aetiology and treatment of pruritus vulvae. E. Vaysièrre.
2. The surgical treatment of pruritus vulvae. G. Cotte.

No. 4, October 1937.

Reports of the discussions of the papers presented at the Congress.

THE TREATMENT OF URINARY INCONTINENCE IN WOMEN.

Muret and Rapin, of Lausanne, discuss the pathology of stress incontinence in parous women. They consider the underlying lesions may be divided into two groups. The incontinence may be due to prolapse of the anterior vaginal wall at the level of the upper end of the urethra dragging the posterior wall of the internal meatus backwards from the anterior wall, which is fixed in front to the symphysis pubis. The other lesion which may be responsible for the incontinence is a direct injury to the vesico-urethral sphincter.

The authors give a comprehensive description of the various operative techniques which have been devised, including anterior colporrhaphy; T-suture of a longitudinal vaginal incision; purse-string suture of the bladder's neck; Kelly's operation for direct repair of the injured sphincter over a Pezzer sound; Marion's modification of the Kelly procedure; Stoeckel's method of direct suture of sphincteric tears after cystoscopic investigation; Halban's operation, in which no search is made for torn muscle fibres, the vesico-vaginal fascia being used to repair the defect; Franz's technique for the utilization of strips of the sphincter ani externus; and, finally, the operation described by one of the authors, Rapin, based on a technique described by C. Roux. In this operation a small suprapubic incision is made. A needle is passed downwards behind the pubis alongside the urethra, emerging by the side of the meatus. One end of a silk thread is drawn up and tied to the other end similarly introduced along the other side of the urethra. The authors use this operation in cases in which there is little or no prolapse present and in cases of failure of plastic procedures. They claim that the urethra is shortened, the meatus displaced forward and slight degrees of anterior vaginal prolapse are cured.

For cases in which large urethral defects are present and a simple plastic procedure is considered unsuitable the operation of pyramidalis transplantation, described as the Goebell-Frangenheim-Stoeckel technique, is recommended. In this operation a flap is made of the lower parts of the recti and pyramidalis muscles, turned down and bisected. The bladder is freely separated from the back of the pubis. A vaginal incision exposes the neck of the bladder, the two flaps are drawn by forceps downwards and backwards around the neck of the bladder and sutured together behind the sphincter.

The paper is furnished with an extensive bibliography.

THE TREATMENT OF VESICO-VAGINAL FISTULA.

C. P. André contributes a general review of the methods available for the repair of vesico-vaginal fistulae. He describes in detail the techniques of the various operations. The paper well merits consultation, though it is too detailed to be abstracted in detail.

For low obstetrical fistulae vaginal repair with a temporary cystostomy is recommended. In the case of post-operative fistulae the transvesical route of approach is recommended. The transperitoneal approach gives a high percentage of cures but carries grave risks of peritoneal infection. When a very large fistula also involves the urethra, the formation of an artificial urethra by means of an indwelling trocar passed into the bladder from a point below the pubis after complete closure of the fistula and the performance of suprapubic cystostomy appears to give better results than the more complicated plastic procedures. Utilization of the cervix or body of the uterus to close large fistulae has never been practised in France. Colpoclysis is not viewed with favour by the author.

THE PATHENOGENESIS AND TREATMENT OF ACCIDENTAL HAEMORRHAGE.

Couvelaire opened the discussion on accidental haemorrhage with a review of the pathenogenesis of the condition. His general conclusion is that no theory so far devised is satisfactory.

A. Weymeersch and J. Snoeck, of Brussels, discuss the question of treatment. They have collected from the literature 1,080 cases of accidental haemorrhage in which trauma could be excluded as a cause. In 79 per cent delivery was effected vaginally, with a maternal mortality of 6.58 per cent; in 21 per cent abdominal section was performed, with a mortality of 21 per cent. The total maternal mortality was 9.44 per cent.

The total foetal mortality was 63.35 per cent, 61 per cent with vaginal delivery, 70 per cent with abdominal delivery. Only 14 patients were delivered by *accouchement forcé*, version, forceps, embryotomy after manual dilatation of the cervix; there were 9 maternal deaths, a mortality of 60 per cent, in this group of cases. Vaginal Caesarean section gave a mortality of 31 per cent. These figures were confirmed by an examination of a further separate series of 102 cases. Conservative Caesarean section gave a mortality of 15.7 per cent (27 deaths in 171 cases), Caesarean section followed by hysterectomy a mortality of 28.5 per cent in 42 cases, Caesarean hysterectomy *en bloc* a mortality of 50 per cent in 14 cases.

No exact relation could be established between the extent of the lesion and the maternal mortality rate. The authors speak well of the use of

pituitrin to determine the presence or absence of potential uterine contractility in considering whether to perform abdominal section or not.

The prognosis of subsequent pregnancies is interestingly discussed on the basis of data supplied by 13 observers. It would appear that the chances of subsequent pregnancies proceeding normally are higher than is generally thought. In a paper by Portes, published in 1935, and based on an analysis of his own and Couvelaire's cases, it was stated that only 15 living children were born in 60 subsequent pregnancies.

The general conclusion of the authors is that the use of radical surgical measures for accidental haemorrhage should be abandoned.

THE AETIOLOGY AND TREATMENT OF PRURITUS VULVAE.

Vaysièrre opened the discussion on the third major subject under discussion, "pruritus vulvae and its treatment". His paper was based both on his own material and that supplied by most of the French gynaecologists. All the methods of treatment are reviewed and discussed in detail. The original paper contains many interesting clinical points, touches on the nicer points of treatment, and well merits consultation in the original. He summarizes the principles underlying the treatment of pruritus vulvae as follows:—

1. *Emergency treatment.* Palliative local therapy should be used only to ameliorate symptoms while the cause is under investigation. Among the many palliative methods available cold, slightly acid baths of short duration followed by thorough drying, the use of lotions of 1 per cent phenol and chloral hydrate used last thing at night, the baths and lotions to be followed by the application of sterilized talcum powder.

2. *Determination of the cause.*

3. *Dangers in treatment.* Local treatment should not be persevered with until the condition becomes chronic. Bathing must not be overdone, as water aggravates most cutaneous lesions. Any treatment provoking local congestion must be avoided. The application of caustics and antiseptics is dangerous. Simple remedies should be tried first.

4. *Idiopathetic pruritus.* This diagnosis should never be made without full consideration.

5. *Special varieties of pruritus.* (*a*) *Pruritus of pregnancy.* A local infection is usually present in this type of case; it responds best to the local application of antiseptics, e.g. silver nitrate, 1 in 2,000. (*b*) *Pruritus due to local infection.* In this group removal of the cause is essential. (*c*) *Pruritus due to hormonal changes.* The intramuscular injection of dihydrofolliculin benzoate in a dosage ranging from 1,000 international units up to 50,000 international units is recommended. Hormonal treatment must be persevered with for at least two months before failure is acknowledged.

6. *Associated treatment.* The treatment of diabetes, syphilis, and other general diseases must receive consideration.

7. *Special treatment.* In this group are radiotherapy, surgery, and neurological methods.

G. Cotte discusses the role of surgery in the treatment of pruritus vulvae. At the outset he stresses the importance of persevering with conservative treatment before resorting to surgery, avoiding rushing from one form of treatment to the other; a practice due as often as not to the distraction of the

patient who "lasse de toujours se gratter, va frapper à plusieurs portes à la fois". Cotte's general opinion is that if cases of local leucoplakia are excluded the results of excision of the vulva are unsatisfactory. Partial excision may be indicated when there is a well-localized vulval lesion causing the pruritus. Total excision is indicated only in women past the menopause; it should not be performed if there is any suspicion of kraurosis, for in such a case the additional scar tissue resulting from the operation will aggravate the symptoms. Division of the internal pudic nerve is commended. The beneficial results are attributed to the section of the sympathetic filaments now recognized to pass along this nerve. The operation is best reserved for women past the menopause. If the whole nerve is divided before its division into superficial and deep branches, the whole vulva is desensitized, while division after it has given off its deep branch may not relieve the pruritus in the anterior part of the vulva. Cotte prefers resection of the presacral nerve, an operation which he has done 5 times, with 2 complete cures, 2 incomplete cures, and one failure, which afterwards responded well to resection of the internal pudic nerve.

P. Malpas.

Bruxelles Médical.

Vol. xvii, No. 48, September 26th, 1937.

The problem of syphilis in rural surroundings. L. Dekeyser.

*Accidents during attempts at the induction of abortion. R. Karhausen.

Vol. xvii, No. 49, October 3rd, 1937.

The treatment of gonorrhoea with sulphanilamide. E. Taut.

The problem of syphilis in rural surroundings (contd.). L. Dekeyser.

Vol. xvii, No. 51, October 17th, 1937.

The development of syphilis in the natives of Morocco since the introduction of modern treatment. E. Lepinay.

Tenth Congress de l'Association des Gynécologues et Obstétriciens de langue française, September 30th, 1937. A report of the proceedings.

Second internal congress on blood transfusion, September 29th, 1937. A report of the proceedings.

Vol. xvii, No. 52, October 24th, 1937.

*Luteinoma of the ovary. R. Bourg and M. Rocmans.

Tenth Congress de l'Association des Gynécologues et Obstétriciens de la langue française. A report of the proceedings (contd.).

Vol. xviii, No. 1, November 7th, 1937.

*A case of haematocolpos due to hymenal occlusion, with radiography. R. Schockaert.

Vol. xviii, No. 2, November 14th, 1937.

*Indications and methods for terminating pregnancy in cases of pulmonary tuberculosis. A. Brindeau.

*Conservation of pregnancy in pulmonary tuberculosis. O. Dauwe.
Société Belge de Gynécologie et d'Obstétrique. The report of the meeting held July 3rd, 1937.

Vol. xviii, No. 4, November 28th, 1937.

The Société Belge de Gynécologie et d'Obstétrique. The report of the meeting held November 6th, 1937.

Vol. xviii, No. 5, December 5th, 1937.

A case of congenital absence of the left half of the diaphragm in the newborn. J. Snoeck.

ACCIDENTS DURING ATTEMPTS AT THE INDUCTION OF ABORTION.

The writer describes the case of a woman aged 37, on whom criminal attempts to induce abortion were carried out one week after a menstrual period had been missed. The uterus was curetted without anaesthesia. A left tubal pregnancy had been removed 10 years previously; she had had syphilis.

One month after the attempt at criminal abortion, she was admitted to hospital because of persistent bleeding. Her temperature was normal and pelvic tenderness, previously present, was only slight: a swelling of the right appendage was palpable. Three weeks later there was a large tumour on the right of the uterus; the Zondek-Aschheim test was negative. Pyrexia developed and laparotomy was performed under spinal anaesthesia. An unruptured right tubal pregnancy and a large blood cyst of the right ovary, firmly adherent to the uterus, were found. Subtotal hysterectomy and right salpingo-oöphorectomy were carried out, and it was then found that the cyst of the ovary communicated with the uterine cavity, as a result of previous instrumental perforation of the uterus.

The author considers that the cyst of the ovary was due to degeneration of the corpus luteum, and that the curettage probably killed the ectopic ovum.

LUTEINOMA OF THE OVARY.

When first seen by the author, the patient, aged 25, complained of menorrhagia of three months' duration. Menstruation had previously been regular and she had 1 child aged 1 year. On examination a small nodular swelling of the left ovary was palpable. The patient refused operation for one year and during that time her menstrual cycle became normal at first, but later she had continuous bleeding alternating with amenorrhoea. These latter symptoms at one time suggested the diagnosis of ectopic gestation. Under spinal anaesthesia, curettage and laparotomy were performed and the left appendage was removed. The left ovary was replaced by an adherent nodular and hard tumour the size of a hen's egg. On section it had the appearance of a fibroma with the exception of the presence of yellow areas and a cavity in the centre.

Microscopic examination showed the tumour to consist of lutein cells separated by connective tissue: the cells contained granules which stained with soudan III. The endometrium showed glandular hyperplasia in the interval phase.

The diagnosis in this case was made on the appearance of the cells and the associated menstrual disturbance. The writer concludes that this is an innocent tumour which was functional and produced oestrin. The necessity for staining sections of ovarian tumours with muci-carmine and soudan III is emphasized.

A Case of Haematocolpos due to Hymenal Occlusion, with Radiography.

A girl of 13 complained of periodic attacks of abdominal pain for 9 months. She had never had evidence of menstruation although secondary sex characteristics were developed. On examination a bulging imperforate hymen was apparent, and a cystic swelling was palpable per rectum. Twenty cubic centimetres of a 15 per cent solution of sodium iodide were injected into the cystic mass and an X-ray photograph was taken 20 minutes later. The radiograph is reproduced and shows dilatation of the vagina, mostly affecting the upper part.

Discharge of the fluid ceased five days after incision of the hymen and subsequent menstruation was normal.

Indications and Methods for Terminating Pregnancy in Cases of Pulmonary Tuberculosis.

The problem of pregnancy complicating pulmonary tuberculosis is a difficult one. Divergent views as to the effect of pregnancy on the pulmonary condition, and as to treatment have arisen because of two methods of approach (i) assessment of statistics; (ii) purely clinical observation on individual cases. Moreover, some physicians deal only with patients under ideal conditions in a sanatorium, whereas others draw their conclusions from observations on patients living in an unsatisfactory environment, and receiving inadequate treatment.

The frequency of pregnancy and phthisis varies from place to place and statistics are inaccurate. In large cities, pulmonary tuberculosis is probably present in 1 out of every 100 pregnant women.

In forecasting the effect of pregnancy in these cases, several factors need consideration: the activity of the pulmonary lesion, the duration of the disease, the social conditions and parity of the patient, the duration of pregnancy, and the history of previous pregnancies.

One hundred and fifty-three cases are recorded in detail; they are divided into four groups.

(*a*) *Acute phthisis with broncho-pneumonic distribution.* Twelve patients in this group all died within six to eight months of pregnancy. Four were treated by induction of abortion, eight by conservative measures.

(*b*) *Sub-acute forms of phthisis.* Of 60 patients, 46 were treated conservatively and of these 11 died and 6 showed deterioration after pregnancy. Therapeutic abortion was practised in 14 cases and 5 of the patients died.

(*c*) *Fibro-ulcerative forms.* There were 44 cases of this type. Twenty-eight patients were treated without interference with the pregnancy and 17 died. Abortion was induced in 16 cases and 4 of the patients died.

(*d*) *Discrete fibro-calcified forms.* Thirty-seven patients came under this heading and all were treated conservatively; there were not any deaths but in 25 per cent there was evidence of reactivation of previously quiescent lesions.

The author stresses that the need for therapeutic abortion is becoming more rare and that medical treatment should be tried in all cases. This necessitates admission to a sanatorium and pulmonary collapse therapy. During labour, delivery should be assisted with the forceps.

Induction of abortion should be carried out if additional complications, such as cardiac or renal disease or excessive vomiting, are present.

Induction of abortion should not be performed if the pulmonary condition is hopeless, if the pulmonary lesion is quiescent, or if the pregnancy is of more than 16 weeks' development.

Induction of abortion may be indicated if the tuberculosis affects both lungs; if pneumothorax is ineffectual, or if conception occurs quickly after lactation during which the phthisis became activated.

If interference is required, the uterus should be surgically evacuated. Local or regional anaesthesia is advocated and described; the products of conception are best removed by dilatation of the cervix or vaginal hysterectomy. Pre-operative and post-operative treatment in a sanatorium is of prime importance.

CONSERVATION OF PREGNANCY IN PULMONARY TUBERCULOSIS.

Dauwe quotes Brindeau's figures (*vide supra*) for groups *b* and *c* and points out that, with medical treatment the mortality was 37.9 per cent. whereas when abortion was induced the mortality was 30.0 per cent. He emphasizes that although by surgical intervention eight mothers' lives were saved, 30 foetal lives were lost.

Dauwe gives details of 84 pregnancies occurring in 63 patients. Two groups are recognized.

(1) *Incurable hopeless cases.* There were 11 patients in this group, all of whom died. Twenty-seven per cent of the children lived.

(2) *Active or quiescent cases, presumably curable.* Fifty-two patients who had 73 pregnancies fell into this group. All were treated conservatively and only 3 died. Fifty-seven live children were born at term.

Several of these patients were gravely ill and detailed case records are given; yet with conservative treatment their response was excellent.

The thesis is put forward that it is legally and socially wrong to destroy the life of the unborn child under any conditions, and, above all, in pulmonary tuberculosis. Induction of abortion is an operation the seriousness of which is not sufficiently emphasized, and reported results in phthisis (16 to 30 per cent mortality) cannot compare with the 5.8 per cent mortality recorded here for conservative treatment. Conservatism is the keynote of progress in gynaecology and obstetrics.

In addition to the usual methods for dealing with pulmonary tuberculosis, the writer advises the intravenous administration of calcium gluconate during pregnancy.

J. N. A. Jeffcoate.

Annali di Ostetricia e Ginecologia.

Vol. lix, No. 11, November 30th, 1937.

*Hysterosalpinography in differentiating the types of ectopic pregnancy. Bortini.

Urinary modifications in the menstrual cycle and in the puerperal state. Donedda.

A rare case of congenital suprarenal cyst in a foetal monstrosity. Its possible relation to dysencephalic splanchnocyst. Ciulla.

Hypogalactia and Marconi therapy. Dogliotti.

HYSTEROSALPINGOGRAPHY IN DIFFERENTIATING THE TYPES OF ETOPIC PREGNANCY.

The generic diagnosis of ectopic pregnancy can be made by simple radiography, but the site is now always determined with absolute certainty in the early stages. Bortini reviews characteristic radiographic signs obtainable by this method. He then describes those gained by other investigators and by himself in hysterosalpingography (Wlassow's method, *Monatsschr. f. Geburtsh. u. Gynäkol.*, 1936, 102–22). An almost certain diagnosis is formed not only of ectopic gestation, but of all its varieties, and any eventual pathological complications. He gives an account of his own cases, illustrating them by photographs and showing how subsequent operations confirmed the results of examination. He insists on the necessity of a long radiological examination and the taking of numerous radiograms.

He thinks the method should be confined to cases of doubtful diagnosis, carried out with every aseptic precaution, and in readiness to intervene by operation immediately, should this be required by incidents arising during examination.

J. H. Filshill.

Revista Italiana di Ginecologia, Bologna

Vol. xx, No. 5, October 1937.

*Moral, medical and judicial aspects and problems in the cure of sterility with particular reference to artificial insemination. Abruzzese.

*Anti-toxic function of the liver in the puerperal state, tested by santonin. Bortolucci.

Another piece of anatomical evidence in favour of endo-uterine nidation of the human ovum. D'Erchia.

Research on the content and elimination of iron in human milk. Martines.

Determination of diastase in the blood as a diagnostic means of pancreatic malfunction in pregnancy. Zambonini.

Anatomical and pathological study of congenital teratoma in the sacrococcygeal region. Vignocchi.

MORAL, MEDICAL AND JUDICIAL ASPECTS AND PROBLEMS IN THE CURE OF STERILITY WITH PARTICULAR REFERENCE TO ARTIFICIAL INSEMINATION.

"No problem regarding the moral and physical well-being of the race or nation is of secondary importance, particularly now, when some and far-

seeing Italian directive politics are devoting greater attention and care to the demographic factor. . . . The Fascist State attributes equal, probably greater, importance to the improvement of the race than to its numerical increment."

On this basis, Abruzzese discusses the moral and legal aspects of curing sterility, referring to artificial insemination and mentioning three cases in which this procedure was requested. In all the aim was pecuniary advantage and involved deceit. Abruzzese condemns the method, and deprecates the cure of sterility in many cases in which resulting numerical increment would be a tax on the State and no benefit to it.

ANTITOXIC FUNCTION OF THE LIVER IN THE PUERPERAL STATE, TESTED BY SANTONIN.

After reference to the numerous methods and results of research on the diverse activities of the liver and their changes in pregnancy, Bortolucci describes his own investigation of its antitoxic function. He has employed a method, recently advocated by Picard, that of Monkhtar and Djevat, called the santonin test. Bortolucci describes its simple technique, illustrating results by graphs, the ordinates of which represent the concentration of santonin, the abscissae the time.

Santonin given by the mouth traverses the stomach unchanged, is dissolved and absorbed in the intestine and carried to the liver. Here it undergoes oxidation forming the yellow substance oxysantonin which appears in the bile and the urine about an hour after administration. The investigation was carried out on about 80 patients. Ten normal non-pregnant cases served as controls, about 40 were tested in early pregnancy, at term, during labour and in the first days of the puerperium, 15 cases were pathological, some suffering from hyperemesis, others from albuminuria.

Bortolucci's results favour the conclusion of other investigators, that pregnancy lowers the hepatic antitoxic function. This malfunction does not appear in the first months of normal pregnancy, is slight at term, becomes more evident during labour, and disappears during the first few days of the puerperium. In cases of gravid toxaemia, the test indicates notable hepatic malfunction at all epochs, and in some cases continues even during the puerperium. The possible influence of the renal factor in the elimination of santonin must not be forgotten in albuminuric cases, although it is negligible in cases of hyperemesis. An associated renal lesion gives a greater irregularity in the curve of the graph.

J. H. Filshill.

Archivio di Ostetricia e Ginecologia

Series 2A, Vol. i, No. 6, November and December 1937.

*The presence of hypoglycaemic and hyperglycaemic substances in the foetal pancreas. Moracci.

The influence of sexual hormones on the blood-vessels. Caffo.

The vaso-constricting action of aqueous foetal suprarenal extracts. Gambino.

The value of Kossiakoff's reaction in the early diagnosis of pregnancy. Tortora.

Voluminous pseudo-cystic myosarcoma, intraligamentous in development. Guarna.

Diseases of newly born infants of obstetric origin. Cappelani.

THE PRESENCE OF HYPOGLYCAEMIC AND HYPERGLYCAEMIC SUBSTANCES IN THE FOETAL PANCREAS.

Moracci refers to the problem of the functional capacity of the pancreas in intra-uterine life as a gland of internal secretion, and to investigations carried out by many authors.

Carlson and Drennan found that in an animal after the pancreas was removed late in pregnancy glycaemia did not occur up to the moment of parturition. They attributed this to passage across the placenta into the maternal organism of hormone from the islets of Langerhans in the foetal pancreas.

Moracci undertook research to show that there were differences of functional endocrine pancreatic activity in two conditions, deducing these from comparison of the body-weight and the epoch of development.

From the pancreas of foetûs at term subjected to Sordelli's process for insulin extraction, a substance was isolated which caused a diminution of the glycaemic percentage in the rabbit. On the other hand, from the pancreas of premature foetûs (at the twentieth week or later) a substance was similarly obtained which caused an elevation of the glycaemic percentage into a rabbit.

Research shows, therefore, that in foetal life there is pancreatic elaboration of substances with a hyperglycaemic action. This appears to prevail over the antagonistic substance (insulin) from the twentieth to the thirty-second week. In foetûs at term the hypoglycaemic action of insulin becomes evident. Further research is required for exact knowledge of foetal pancreatic function.

J. H. Filshill.

Atti Della Societa Italiana di Obstetricia e Ginecologia.

Vol. xxxiii, Supplement No. 1, January and February 1937.

*The substitution of certain vegetable extracts for folliculin. Mornigliano.

*The dangers of the cumulative effect of digitalis and calcium. Cattaneo.

*Multiple pigmented cutaneous fibromata in pregnancy. Consoli.

Vol. xxxiii, Supplement No. 2, March and April 1937.

*Oestrogen hormones of vegetable origin. Mornigliano.

Vol. xxxiii, Supplement No. 3, May and June 1937.

*Primary intractable epistaxis during pregnancy. Fronticelli.

THE SUBSTITUTION OF CERTAIN VEGETABLE EXTRACTS FOR FOLLICULIN.

The high cost of folliculin and the difficulty of obtaining sufficient material for its extraction has led to attempts at its synthetic manufacture,

or to extraction from some vegetable substance with corresponding biological action.

Synthetic fabrication has not been free from technical drawbacks. Obtaining a vegetable extract is a much simpler process. In 1930 Mornigliano began experiments with oils extracted from seeds rich in oestrogenic material and his results encouraged optimism. He describes, with illustrations, the uterine changes in immature rats after injection of varying doses of these oils.

The uterine horns, primarily thread-like and still so in the control animals, are rapidly and enormously enlarged. The minimal quantity of oil injected was 0.5 c.c., the maximal 2 c.c.; the interval of control was only 100 hours. The same results are seen after the injection of 2,000 to 3,000 international units of folliculin.

It is an interesting fact that distension is due to fluid and not so much to hypertrophy of the uterine walls. The uterine horns show the typical aspect of a hydrometer. Further experiments may prove that diminution in the quantity of extracts injected and a greater interval of time would yield modifications corresponding to those induced by the injection of folliculin.

THE DANGERS OF THE CUMULATIVE EFFECT OF DIGITALIS AND CALCIUM.

Cattaneo describes a clinical fatality due to the superimposed effect of the intravenous injection of calcium after that of digalen. The patient, though prone to hysterical attacks, was in fairly good health and had been successfully operated on for vaginal prolapse. Because of post-operative tachycardia, nervous irritability and sleeplessness, she had been given injections of 1 c.c. of digalen twice daily with 1 c.c. of antopon at night. On the fourth night, because of hysterical symptoms, 1 c.c. of calcium bromide was substituted for the antopon. Symptoms of cardiac and respiratory difficulty immediately followed. These passed off under treatment, but returned 6 hours later and then the patient died. The post-mortem examination showed no apparent cause of death save myocardial flaccidity.

A few days after Cattaneo noticed a report of a similar case published by Bower and Mengle in *The Journal of the American Medical Association*. Digalen had been given after an operation for cholecystitis to correct tachycardia. Thinking the condition might be due to sympathetic disequilibrium, a colleague advised an injection of calcium gluconate. Two minutes after the injection the patient died. Bower and Mengle refer to another case in which Richter records the fatal effect of an injection of calcium chloride following two days' treatment by injections of digalen. Bower and Mengle have since carried out experiments on animals to ascertain the possible cause of cardiac collapse. Given alone, calcium gave rise to transient weakening of the pulse and transient lowering of the blood-pressure. When preceded by the injection of digitalis in therapeutic doses, the dose of calcium corresponding to 30 to 40 per cent of the minimal lethal dose caused cardiac fibrillation and death.

The precise interaction of the two salts remains a matter for chemists to solve. In view, however, of the recent widespread use of calcium injections, it is well to remember that these may be dangerous or fatal in combination with digitalis.

Multiple Pigmented Cutaneous Fibromata in Pregnancy.

In 1882 Recklinghausen described a disease of which the three main features were cutaneous and subcutaneous tumours, pigmentation of the skin and multiple tumours of nerves. The most serious complications were local and mental nervous disturbance, bony deformities, and malignant degeneration of the small tumours.

Niskizaki in 1928, illustrating pigmentation of the skin in relation to toxaemia of pregnancy, connected the origin of Recklinghausen's disease with pregnancy. Later, Ferrero and Cucco reported cures of Recklinghausen's disease by homoplastic ovarian grafts.

Consoli describes a case in which multiple cutaneous fibromata, noticed by the patient from her childhood, grew much larger in size and more numerous in distribution during the fifth month of her first pregnancy. This ran a normal course, but the cutaneous condition remained unaltered. The child, nursed by its mother, had eczema of the scalp and erythematous spots over its body. Consoli considers the case one of Recklinghausen's disease, though nervous symptoms were completely absent. Pregnancy he regards as a contributory, not an originating, factor. He learned that there was a family history on the male side of pigmented tumours of the skin. But, in view of the disease's growing worse during pregnancy and remaining unchanged after it, there is no certainty of its disappearance. It is possible that it may give rise to bony deformities in succeeding pregnancies. In an early pigmented stage it might be confused with Addison's disease, which sometimes is a complication of pregnancy.

Oestrogen Hormones of Vegetable Origin.

Mornigliano now publishes, with illustrations, the results of injections of vegetable oestrogen hormones and of folliculin in castrated rats. The histological changes in the uterus and vagina and the appearance of oestral phenomena are seen after both types of infection.

In the first series the earliest interesting changes concern the epithelium, showing rapid development of projections and invaginations. The glandular elements multiply with proliferation of the cells and then increased secretory activity. With injections less than 0.5 c.c. proliferation is greater than secretion. A dose of 2 c.c. produces a greater change than 10,000 international units of folliculin in oily solution. The modifications induced by progynon are less in these than those due to vegetable extracts, though still imposing in relation to control uteri. Modifications after vegetable extracts are short in duration. In 10 days the histological picture scarcely differs from the normal one. In the ovaries of immature animals changes are noted indicating maturation and luteinization of the follicles.

In vegetable extracts folliculin-like substances seem to be associated with others which act like the hormones of the anterior hypophysis.

It emerges from the experimental results that oestrogenic activity superior to that of extracts now in use may yet be found which will successfully compete with oestrogenic hormones from the urine or ovary.

Primary Intractable Epistaxis During Pregnancy.

The functional and anatomical changes of the mucosa of the pituitary

gland connected with menstruation and pregnancy often cause congestion of the nasal mucosa and epistaxis in certain individuals. A greater variation in reflex pituitary phenomena occurs during pregnancy, but epistaxis is infrequent, and usually symptomatic of other diseases, such as hypertension, nephropathy, or anaemia. There is, however, a category of idiopathic nasal haemorrhage in which the prognosis is grave, since intractable haemorrhage may lead to death from acute anaemia. Fronticilli describes two cases one of which ended fatally.

Case 1. There was no history of epistaxis before the actual pregnancy in the first case. The patient was a primigravida, aged 23 years. Epistaxis began during the fourth month. Temporary cessation was obtained by the usual means—plugging, etc.; but directly the plug was removed bleeding recurred. The haemorrhage ceased only when the pregnancy was terminated by vaginal hysterectomy at the twenty-fourth week, but the patient died from acute anaemia on the eighth day of the puerperium.

Case 2. In the second patient epistaxis began at the thirty-sixth week of pregnancy. Labour was immediately induced when the alarming nature of the haemorrhage was recognized. In 24 hours epistaxis ceased. The patient made a good recovery. In neither case was there a tumour in the nasal fossa. The haemorrhage evidently came from the whole tract of the nasal mucosa.

J. H. Filshill.

Archiv für Gynäkologie.

Band 164, Heft 3.

*Hormonic influence of the foetus on labour. S. Tapfer.

*Induction of pathological modifications in the mucosa of the uterus and cervix in apes. A. Migliavacca.

*Hormone researches in arrhenoblastoma. Z. v. Szathmáry.

The effect of caffeine on ovarian function in white mice. J. Bahr.

*Malignancy in granulosa-cell tumours. H. Hückel.

*Tuberculosis of the human and of the cow's placenta in connexion with the occurrence of congenital tuberculosis. L. P. H. J. de Vink.

*Masculinization and feminization, in connexion with lutein cell tumours of the ovary. J. Novak and O. Wallis.

*Differential diagnosis of adenoma malignum cervicis. A. Slany.

The daily consumption of vitamin C during pregnancy. G. Gaehtgens.

The placental content in carotin and vitamin A. G. Gaehtgens.

The significance of the blood-picture during the menstrual cycle. O. Bokelmann.

Haematological investigations in protracted treatment by sexual gland hormones. W. Wobker.

The normal variability of the human menstrual interval. J. Björnsson.

*Terminal arborizations of vegetative nerve tissue in the healthy and inflamed Fallopian tube. J. Beaufays.

A hamartoblastoma of the placenta: diffuse angioblastoma. J. Beaufays.

Band 165, Heft 1.

Neuro-hormonal regulation of renal function during the administration of large amounts of water during pregnancy. Part 1: Normal pregnancy. G. Effkemann.

*Experimental researches concerning the physiology and pharmacodynamics of the Fallopian tube. C. Cella and I. D. Georgescu.

Rare abnormalities of the umbilical vessels. W. Rust.

Feeding tests with vitamin C in nursing mothers. G. Gaehtgens and E. Werner.

*Fractures of the skull in the newborn and their clinical significance. J. Erbslöh.

The duration of labour and its dependence on climatic and geographical influences. K. Nordmeyer.

*The sexual cycle in the vagina of the newborn during the genital crisis. N. Zaharescu-Karaman, M. Alexiu, and A. Ursu.

The functional condition of the liver in inflammatory diseases of the female genitalia. A. N. Sulimowa and W. P. Umnowa.

HORMONIC INFLUENCE OF THE FOETUS ON LABOUR.

After mentioning the demonstration of placental and pituitary uterus-stimulating hormones, and summarizing experimental work seeking to explain in terms of endocrine forces the determination of labour, Tapfer points out that the surviving guinea-pig's uterus is not altogether a suitable medium for research. French writers' finding that the rectal administration 10 days before term of urine from parturients was speedily followed by labour has been confirmed. That pituitary secretions are not all-important in all species is shown by the occurrence of labour at term in rats after hypophysectomy (P. H. E. Smith). Anti-oxytocic enzymes from corpus luteum and placenta have been envisaged, with the support of much experimental evidence which is here very critically reviewed. Possible anti-oxytocic influences from the foetus have been too little considered. Evidence of their existence has been found by Tapfer in the fact that the serum of pregnant guinea-pigs inhibits the pituitrin response in the virginal guinea-pig's uterus: the maternal serum has a similar effect, the source of the hormone here concerned probably being the foetus. After birth the inhibitory effect persists longer in the foetal than maternal serum. The onset of labour is to be regarded, it is said, as determined by the preponderance of utero-stimulant hormonic factors, among which folliculin is important by reason of its increasing the sensitivity to pituitrin, over utero-inhibitant hormones produced by the foetus.

INDUCTION OF PATHOLOGICAL MODIFICATIONS IN THE MUCOSA OF THE UTERUS AND CERVIX IN APES.

In *macacus rhesus* and *patio amydras*, a month after castration, which is followed by an increased excretion of prolan A, 60 units of follicular hormone were injected daily for 21 to 61 days. In the cervix the epithelium showed a compact or vacuolated syncytial structure, and zones of squamous epithelium were noted. The squamous epithelium was more probably derived from heteroplastic changes in the reserve basal cells of the cylindrical epithelium than from ingrowth from the cellular investment of the portio.

Squamous epithelium was not found in the corporeal endometrium, although Migliavacca found it there in similar experimental conditions in rats.

HORMONE RESEARCHES IN ARRHENOBLASTOMA.

At the time of operation for twisted ovarian tumour complete hormone examinations could not be made, but from the fact that the urine, in a patient aged 25 years, contained no folliculin or only traces of that substance, and since the secondary sexual characteristics had recently been transformed in a masculine direction, an arrhenoblastoma was correctly diagnosed. After operation those characteristics reverted to the feminine type, and three months later the urine contained 130 mouse-units of folliculin per litre, and the menses, after 18 months' suspension, returned. A recurrence of the tumour, a year and a half after this, was accompanied by renewed hirsutism: the urine contained the male sexual hormone in slightly increased percentages, and folliculin could not be found either in the urine or the tumour recently removed. Three months before death gonadotropic hormone was absent from the urine, which now contained 1,700 units of follicular hormone per litre and only 10 units of male hormone. In the original tumour epithelial strands predominated over sarcomatous tissue; in the second this was reversed.

MALIGNANCY IN GRANULOSA-CELL TUMOURS.

More prolonged observation may show that a larger proportion of granulosa-cell tumours is malignant than is usually thought. Six cases have been reported in the German literature of recurrences after 6 to 14 years. In Hückel's case a local recurrence, speedily followed by metastasis and death, occurred, without menstrual disturbance, 14 years after unilateral removal of the adnexa for apparently benign granulosa-cell tumour in a woman aged 22 years. Metastases were confined to the peritoneum and the neighbourhood of the primary tumour. In contrast with others this case of granulosa-cell tumour proved to be refractory to X-radiation. Although a certain degree of masculinization often accompanies these tumours, it may be held, as in this case, not to be causally connected, but to be due to an accompanying defective sexual differentiation. More radical operative treatment should be seriously considered, even in young subjects.

TUBERCULOSIS OF THE HUMAN AND OF THE COW'S PLACENTA IN CONNEXION WITH THE OCCURRENCE OF CONGENITAL TUBERCULOSIS.

After reviewing the pathological histology of placental tuberculosis, as described by various authors, in mankind and the cow, and contrasting the discoidal, deciduate, haemochorial human placenta with the multiple, non-deciduate, syndesmochorial placenta in the cow, de Vink endeavours to explain the greater frequency of congenital tuberculosis in the calf than in the human foetus. In the human subject, a proliferative process is seen, with evidence of resistance on the part of the villi; in the ox a destructive exudative process affecting comparatively large surfaces and encountering much less active measures of defence. Another factor is found in the comparatively limited capacity of the cow for aborting.

MASCULINIZATION AND FEMINIZATION, IN CONNEXION WITH LUTEIN CELL TUMOURS OF THE OVARY.

In a single woman, 30 years of age, 2 years' amenorrhoea was accompanied by masculinization of the hair distribution, voice, laryngeal configuration and musculature and enlargement of the clitoris, without psycho-sexual alterations: these changes, together with polycythaemia, increase of blood-pressure and increase of blood-sugar, regressed after the removal of a right ovarian tumour weighing 390 grammes. It was predominantly solid and composed chiefly of tissue macroscopically resembling giant corpora lutea and microscopically containing an abundance of intracellular lipoids. Neither before nor after operation did the urine contain prolan: before, folliculin was absent from urine and blood; afterwards, it was present in the urine. It was not possible satisfactorily to test for the male hormone. Reviewing the question of masculinization in ovarian tumours, Novak and Wallis recall that it has been recorded (1) in tumours classified, according to Robert Meyer, as arrhenoblastomata; (2) in a few cases of large-cell tumours, the so-called lutein cell tumours. The relevant cases of the latter group have numbered 6, and only 3 survive a critical consideration. The literature, therefore, contains 3 cases, that here recorded being the fourth. Schiller, after examining the authors' sections, suggested that the tumour—from the sharp intercellular distinction which it showed and its clear delimitation from the remainder of the ovary, as well as from the polycythaemia, increase of blood-pressure and increase of blood-sugar—might be, like that in one of the other cases, of suprarenal origin. That certain suprarenal tumours cause a reversal of feminine characters is, of course, well known. Schiller recognizes only 2 groups of masculinizing ovarian tumours, arrhenoblastomata and suprarenal tumours: he suggests that lutein cell tumours arise in the cells, known to be present in the ovarian hilus, corresponding to the Leydig interstitial cells of the testis. That a lutein cell tumour, arising in feminine material, should lead to masculinization is more easily explicable in view of the finding of Steinach and Kun that luteinization of the guinea-pig's ovary, after X-radiation or after injection of gonadotropic hormone, is accompanied by considerable enlargement of the clitoris and by psychic masculinization; luteal tissue in the female must contain a male principle as well as the hormone, whose effect on the endometrium is well known.

DIFFERENTIAL DIAGNOSIS OF ADENOMA MALIGNUM CERVICIS.

Slany would preserve the distinction between adenoma malignum and adenocarcinoma. Adenoma malignum, destructive adenoma, although comparatively frequent in the body of the uterus, is rare in the cervix. A case is recorded in which, 8 months after an operation for prolapse, vaginal hysterectomy was done for irregular bleeding. The specimen showed, in addition to a luteal ovarian cyst, a fundal polypus and some degree of adenomyosis interna, a tumour of the cervix consisting of much-branching, cylindrical-cell glandular tissue which only occasionally consisted of more than one layer and gave negative results with mucus-staining reagents. The muscle was deeply penetrated: the proliferation had nowhere led to the formation of solid cell-groups. In the differential diagnosis adenomyosis originating in the corporeal glands is rejected by reason of the regular cell

arrangement and the absence of a muscular or characteristic stromal investment: adenomyosis of the cervical glands from the negative mucicarmine results: and a tumour of remnants of Gärtner's duct from the site in the middle of the posterior wall of the cervix and from the regularity of the epithelial arrangement.

TERMINAL ARBORIZATIONS OF VEGETATIVE NERVE TISSUE IN THE HEALTHY AND INFLAMED FALLOPIAN TUBE.

Beaufays, who, in 1935, with Goecke described an abundant terminal reticulum in the mouse's ovary, has found similar arborizations in the human ovary. He now reports a study of silver impregnation (Bielchowsky-Gros) staining in 36 normal and 12 inflamed Fallopian tubes. A very abundant vegetative nerve supply is thus revealed, a fine syncytial neuroplasmic veil, containing Schwann nuclei, coming into intimate contact with circular and longitudinal muscle fibres, connective tissue and blood-vascular walls, and penetrating the folds of the mucosa, but not the epithelial cells. The reticulum in the connective tissue includes sling territories regarded as afferent endings. In tubal inflammation zones of degeneration are seen in the nerve arborizations, the fibres showing granular disintegration and the Schwann nuclei being vacuolated.

EXPERIMENTAL RESEARCHES CONCERNING THE PHYSIOLOGY AND PHARMACODYNAMICS OF THE FALLOPIAN TUBE.

Examining surviving Fallopian tubes removed from human subjects at operation or from pigs shortly after slaughter, Cella and Georgescu found automatic and truly peristaltic contractions in all sections of the organ, having a rhythm of 2 to 6 a minute, involving both longitudinal and circular fibres, and directed towards the uterus. The activity is diminished during the intermenstrual interval: increased after menstruation. The optimal temperature and hydrogen-ion concentration are 37·75° and pH 7.40 respectively. The Fallopian tube is stimulated by barium chloride, alcohol in small concentrations, and very notably by the mechanical effect of lipiodol: also by nicotin, adrenalin, ergotin, doryl, pilocarpin, and eserin in small doses. Folliculin and corpus-luteum extract have a slightly inhibitory effect on peristalsis: prolan does not have any effect on rhythm, but induces increased sensitiveness to folliculin.

FRACTURES OF THE SKULL IN THE NEWBORN AND THEIR CLINICAL SIGNIFICANCE.

More is known about the clinical features of intracranial than cranial birth injuries, and textbooks teach that gross lesions of the skull are almost immediately lethal. Cranial fractures are at least as common after spontaneous delivery as after operative delivery: in a celebrated case (Frank, 1823) 5 successive children of the same mother were born with a broken skull. Since sutures are absent fracture is usually confined to one bone. The response of the foetus to the fracture can seldom be immediately or continuously observed, for either the time of the accident is unknown, in spontaneous deliveries, or delivery follows immediately after the injury, in operative deliveries. In two cases in which Caesarean section, done on maternal indications, followed several hours, in one case 16½ hours, after

the unsuccessful application of the forceps, the foetal heart-tone was normal until the first respirations after delivery, in spite of very extensive multiple cranial fractures (Schroeder and Holtermann respectively). Erbslöh noted a similar finding in spontaneous delivery several hours after failed forceps. Occasionally, especially when the formation of an external cephalhaematoma compensates for rising intracranial tension, the infant survives extensive fractures for considerable periods (12 hours, Lantuéjoul; 11 days, Esch; 3 months, Reichel). Operations have been done successfully at the ages of 3 months (Reichel), 1 day (Tarpet), and 14 days (Ballance). In a case of fractured parietal bone, following the unsuccessful application of the forceps, treated conservatively, Erbslöh noted normal physical, mental, and radiological signs at the age of 5 years. Uncomplicated injuries of the cranial capsule, i.e. those unaccompanied by intracranial injuries, are extremely poor in symptoms, necessitate no special treatment, and heal quickly: it is probable, therefore, that they are commoner than is usually thought. Only systematic X-ray examinations of all infants who have had a difficult delivery can show the true frequency and the clinical significance of fractures of the skull. In every case in which signs of increasing intracranial pressure develop or in which a compression fracture is present, surgical intervention is rational and affords the only hope of successful treatment. Of late sequelae the only one so far recognized is meningocoele spuria traumatica or traumatic cephalhydrocoele.

THE SEXUAL CYCLE IN THE VAGINA OF THE NEWBORN DURING THE GENITAL CRISIS.

The authors examined smears from the vaginal secretion in 60 unselected female infants twice daily for 10 days after birth. They conclude that the congestive phenomena, sometimes noticeable about the third to sixth days, in the external genital organs and breasts are associated with typical changes, significant of a hormonic cycle, in the cytology of the vaginal secretion. They distinguish (1) from the first to third days normal epithelium; (2) then appearance of microbes and leucocytes; (3) disappearance or diminution of leucocytes, and appearance of single or grouped keratinized cells on the fifth or sixth day; (4) reappearance of leucocytes, in association with slight bleeding, about the eighth, ninth, or tenth day. This "genital crisis" is the external sign of an incomplete utero-ovarian cycle, and is due to hormones of maternal (placental or ovarian) derivation. Its delayed appearance, a few days after birth, is explained by the presence, *in utero*, of an inhibitory hormone—probably the same which neutralizes the folliculin effect during pregnancy.

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*Hormonal treatment of unsatisfactory lactation in women. G. Effkemann

The treatment of puerperal bleeding with folliculn. W. Bauer.

The effect of sexual hormones on the oviducts of sticklebacks. K. Ehrhardt and K. Kühn.

Short report upon further results of inguinal eugenic sterilization. P. W Siegel.

Foetal endocarditis. J. Abraham.

*An interesting case of criminal abortion. K. v. Pallos.

No. 48, November 27th, 1937.

Remarks on the increase of birth length in the newborn. A. Mayer.

The question of diagnosis of latent carcinoma of the portio. G. Mestwerdt.

Findings with the kraniotraktor. W. Neuweiler.

Remarks on Holzbach's work "Uterine incision in the bloodless space of Esmarch." J. Frigyesi.

*Treatment of gynaecological diseases with concentrated gases through the vagina. N. J. Kuschtalow.

No. 49, December 4th, 1937.

Conversion of an extra-insular pregnancy glycosuria into a glycosuria of insular origin. H. Albers.

*The value of purely operative treatment of extensive carcinoma of the cervix. C. Schroeder.

Whether the obstetric and gynaecological education of students is capable of improvement. K. Riediger.

The value of the Kustallow pregnancy reaction with infusoria. A. Uhlich.

The final verdict upon the value of the chemical pregnancy reaction after Visscher-Bowman. B. Belonoschkin.

No. 50, December 11th, 1937.

Correlated observations upon the development of the distal end of the vagina and of the hymen in the human. A contribution to constitutional embryology. R. Meyer.

*The limiting factor of the corpus luteum hormone in the development of epithelial metaplasia. G. Effkemann and L. Herold.

Diagnosis of dysmenorrhoea. P. Singer.

A case of epiphyeolysis of the distal end of the humerus as a rare birth injury. W. Obadalek.

Results with prontosil in obstetrics and gynaecology. C. Wallischeck.

No. 51, December 18th, 1937.

*Delivery after vaginal transplantation of the Fallopian tube in reconstruction of the uterine cavity. P. Strassmann.

*The hormonal causes of postmaturity. A. v. Arvay.

*The question of cardiac function in young human embryos. J. Lukinovic

Eclampsia. W. Hattingen.

Eunarcon in out-patient gynaecological practice. W. Schütz.

No. 52, December 25th, 1937.

*Old multiparae. F. Szolnoki.

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Pregnancy changes in the genital organs of the newborn female. E. Philipp.
Investigations into the vaginal contents in newborn and infants. M. Alexiu and K. Herrnberger.
Fontanelle tension in the newborn. H. Braun.
Illegitimate births. G. K. F. Schultze.
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Colposcopy in the limits of effective fight against cancer. F. Lönne.
A beginner is able to recognize carcinoma of the portio with a colposcope. A. Mönkeberg.
Standards of fractional radiation in female genital carcinoma. H. Kirchhoff.
Our results with the Freund-Kaminer cutaneous reaction for the early diagnosis of carcinoma. R. E. Buchwald.

No. 2, January 8th, 1938.

Obituary—A. H. M. J. van Rooy. F. C. van Tongeren.
The indicated measures for puerperal or operation cases which suffer particular risk from previous thrombosis or embolism. E. Vogt.
Severe thrombosis before delivery as an indication for delivery by Caesarean section. Fr. Isbruch.
That the Fallopian tubes should be totally removed in legal sterilization. B. Ottow.
Pregnancy after tubal resection and end-to-end anastamosis. F. Hanak.
Tubal stump pregnancy. J. Batizfalvy.
Whether the high amputation of the cervix is a sterilizing operation F. Movers.
The significance of the principle of symmetry as a causation of human malformations. H. Kolbow.

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Radiation of benign cases of haemorrhage. V. Probst.
The mechanism of metrorrhagic bleeding in pedunculated myomata. E. Pelkonen.
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Arrest of mammary secretion by follicular hormone. W. Lindemann.
The problem of pregnancy, vesicular mole, chorion-epithelioma and the Aschheim-Zondek reaction. F. Isbruch.
Important forms of disturbance and their hormonal control. W. Rust.
Histological follow-up of the effect of cutaneous administration of follicular hormone for kraurosis vulvae. E. Tscherne.

HORMONAL TREATMENT OF UNSATISFACTORY LACTATION IN WOMEN.

Effkemann refers to animal experiments into the physiology of lactation. From this arose the possibility of increasing the development of the mammary glandular tissue and the determination of the neurohormonal mechanism which pointed to the presence of a lactation hormone.

Experiments were carried out to attempt to increase mammary glandular development during the last months of pregnancy and by this means to

bring about more satisfactory lactation. A combined folliculin corpus luteum hormone treatment of 50 to 60 mg. of oestradiolbenzoate and 20 to 50 mg. of progesteron resulted in profuse lactation in such breasts which previous to treatment had held out no promise of satisfactory function.

AN INTERESTING CASE OF CRIMINAL ABORTION.

v. Pallos describes the case of a patient of 33 years of age who had had 3 normal full-time deliveries and 2 non-febrile abortions. The last menstrual period took place in November 1936 and the expected December period was one day overdue counting her normal menstrual cycle as being one of 28 days. For this reason the patient pushed a well-oiled previously bent piece of wire into the uterus. The wire went in easily but could not be withdrawn by the patient, or by her husband. She therefore walked to her doctor's surgery and he sent her into hospital where she arrived six hours after the introduction of the wire. On the way she had a rigor, her temperature was 37.8°C. and her pulse-rate 88. At the hospital 6 cm. of 2 mm. wire were found hanging out of the external os with the hooked end caught in the posterior uterine wall. All attempts to withdraw the wire were unsuccessful.

In view of the patient's infected condition attempts to remove the wire through an anterior hysterotomy incision were decided against as was laparotomy. The patient was treated by vaginal supravaginal hysterectomy after careful cleansing of the visible part of the wire.

The removed specimen was hardened and sectioned after it had been split down the anterior wall to afford a naked-eye view of the posterior wall with the hooked wire in position. On the posterior wall four deep scarifications were seen and in one of these directed downwards from the fundus for 7 mm. the point of the hook of wire, which measured 19 cm., was embedded.

Histological examination of the uterine wall showed inflammatory changes with beginning necrosis in the neighbourhood of the wounds. At the site of the point of the wire there was a small cavity which the writer considered to be the cavity inside the chorionic sac of a very young ovum which had lost its entire contents, probably as a result of the trauma of the wire's point. The surrounding tissue was so young that the trophoblast had not even yet become differentiated into primary villi though the syncytial tissue was beginning to become aggregated into bundles and pillars. The writer regrets that the ovum could not be identified as he thinks it might have been younger than any so far described.

TREATMENT OF GYNAECOLOGICAL DISEASES WITH CONCENTRATED GASES THROUGH THE VAGINA.

Kuschtalow refers to the use of drugs which will generate gas in the following cases for respiratory diseases, for stimulation of the activity of the skin and mucous membrane and for disinfectant and deoderant purposes.

For some time watery solutions of gases such as carbon dioxide or sulphur dioxide have been used for local application, and since 1918 in America weak solutions of chlorine in air have been employed in the treatment of influenza. Following this idea it has been suggested that the concentrated application of a gas should have a marked effect upon diseased tissue. The

writer has arranged an apparatus for introducing the medicinal gas which is manufactured at the time of use through a Wolff's bottle into a speculum whose outer orifice is sealed by a stopper with three perforations. In addition to the entering tube there is one connected to a hand bellows and one exit tube connected to a bottle containing an absorbant solution. The writer has employed both chlorine and bromine in his treatment of inoperable carcinoma of the cervix in about 20 cases during 2 years. Each seance lasted 10 to 15 minutes and was repeated on several occasions.

He found that the unpleasant odour of these growths practically disappeared and the discharge was lessened. The results were obtained more quickly with chlorine than with bromine. The writer suggests that this method might also well be employed for cases of offensive vaginal discharge of other than malignant origin.

THE VALUE OF PURE OPERATIVE TREATMENT OF EXTENSIVE CARCINOMA OF THE CERVIX.

Schroeder reviews a series of cases operated on in the Charité in Berlin by Wagner during the period July 1928 to July 1931. These cases were nearly all border-line cases. There were 51 cases.

During the period 1928 to 1931 there were in all 293 cases of carcinoma of the cervix; of these the growth was locally operable in 39 cases, but operation was contra-indicated for general reasons and the patients were treated by radiation.

Seventeen of the 51 border-line cases treated by operation were alive and well 5 years later—a five-year cure-rate of 33.3 per cent. Eight patients, or 15.7 per cent, died as a result of the operation; 7, or 13 per cent, developed fistulae, and 1 had been lost sight of.

Of the 39 operable cases treated with radiation 13, or 33.3 per cent, were alive and well after 5 years; 1 patient, or 2 per cent, died as a result of the treatment. The morbidity was nil, and 1 patient had been lost sight of.

During the course of the operation on the 51 cases, on 42 occasions was it found necessary to remove apparently involved glands. In each case these glands were histologically examined, and only in 11 cases were they found to be carcinomatous. The after-history in each of these 9 cases was one of rapid recurrence and death within 5 years.

The cause of death among the 8 patients who died as a direct result of the operation was embolism in 4, circulatory failure in 2, and peritonitis in 2. In comparing the five-year results of operation in these somewhat advanced cases with those of radiation in early operable cases the writer holds that the results are quite satisfactory. The immediate mortality of 15.7 per cent is no worse than that of 16 per cent given by Schröder for Werthiem's operation on early first-stage cases, 239 in number, treated in the Kiel Clinic. He considers the occurrence of fistulae an indication of the advanced type of growth which was treated by operation; the fistulae healed spontaneously in 2 of the 7 cases, the remaining 5 patients died of recurrence within 14 months. In conclusion, it is pointed out that the surgically treated cases, with one exception, were never given any form of radiotherapy. Unless the type of treatment is kept entirely apart it is impossible to attach any value to the results obtained.

THE LIMITING FACTOR OF THE CORPUS LUTEUM HORMONE IN THE DEVELOPMENT OF EPITHELIAL METAPLASIA.

Effkemann and Herold carried out a series of experiments on whole rats to determine the effect of the administration of folliculin and corpus luteum hormone upon the uterine mucosa. When marked hyperplasia of the uterine mucosa had been induced by large doses of folliculin the subsequent administration of corpus luteum hormone caused it to retrogress.

If folliculin and corpus luteum hormone are given together hyperplasia does not occur.

The contribution is illustrated by five photographs of histological sections of the uterine cervix and corpus after such experiments.

DELIVERY AFTER VAGINAL TRANSPLANTATION OF THE FALLOPIAN TUBE IN RECONSTRUCTION OF THE UTERINE CAVITY.

Strassmann describes the case of a young woman of 21 years of age who was delivered of her first child in hospital without any abnormality; she was sent home on the eighth day after delivery. On the fourteenth day her uterus was curetted by her private doctor in her own home for uterine bleeding. After the curetting there was no further uterine bleeding for three months up to the time that she came under the care of the writer. At this time she suffered from sacral and abdominal pain, headache and epistaxis with amenorrhoea.

A sound could be passed for only 1 cm. and the uterine cavity was completely obliterated. The patient was operated on, access to the uterine body being gained through an anterior colpotomy incision. The left Fallopian tube was detached and its uterine end passed through a lateral incision in the uterine body down to the patent cervical canal, where it was fixed with two stitches. The fimbriated end was left opening into the peritoneal cavity.

Her first marriage having been terminated, the patient married again 2½ years after the operation. Menstruation had been re-established 2 months after the operation. The patient became pregnant one month after her second marriage and she delivered herself spontaneously 6 days before the expected day of her confinement of a somewhat under-nourished foetus weighing 2,500 g. and measuring 47 cm.

The third stage of labour was complicated by delay in separation of the placenta with smart haemorrhage after one hour. Half an hour later the placenta partially separated and was expelled by light pressure. One cotyledon had remained adherent and was removed digitally. The puerperium was complicated by intra-uterine sepsis and a rise of temperature. The patient returned home well on the twenty-fifth day. Examination of the chorionic sac showed it to have an abnormal area of placental tissue, about three-fifths of the whole surface was covered with villi. The weight of the placenta and membranes was 400 g. At its greatest thickness the placenta measured 1.5 cm.

The writer suggests that the tubal mucosa served to help the satisfactory embedding of the ovum but that it afforded a less satisfactory blood-supply for its development and thus brought about a diffuse placental development.

in the same way as that in which diffuse development of the placenta sometimes results in placenta praevia.

Fuchs has on seven occasions followed supravaginal amputation of the uterus with transplantation of the Fallopian tube down to the cervical canal and established menstruation without subsequent pregnancy but his patients averaged 39 years of age.

THE HORMONAL CAUSES OF POSTMATURITY.

V. Arvay has carried out a series of experiments on pregnant rabbits to determine whether the administration of various hormonal preparations could result in the prolongation of pregnancy, which in the rabbit is normally 30 days. First he treated 4 pregnant rabbits from the twenty-fourth day with preparations of corpus luteum. Two were given glanducorpin and two proluton. They were given a daily dose of 2 k.e. and this had no marked effect in prolonging pregnancy. Those treated with proluton were delivered between the thirtieth and the thirty-second days and those given glanducorpin between the thirty-first and thirty-third days.

A further series of animals was treated from the fifteenth to the twentieth day with anterior pituitary hormone, being given a daily dose of 50 e. of luteoantin (Richter). Treatment was continued up to the fifty-seventh, fifty-sixth and fiftieth days of pregnancy when the foetûs had died and laparotomy was performed for their removal.

Three other animals were treated with young pregnancy serum (3 to 4 months) from which the folliculin had been removed by treatment with ether. Each animal was given an injection of 10 c.c. of this serum from the twenty-fourth day of pregnancy and pregnancy continued for 31, 18 and 15 days, respectively. Two other animals were given intravenous and subcutaneous injections of pregnancy urine (3 to 4 months) previously treated with ether. Injections of 10 c.c. were given daily from the twenty-fourth day and resulted in overcarrying for 18 and 21 days; the foetûs were dead and macerated.

THE QUESTION OF CARDIAC FUNCTION IN YOUNG HUMAN EMBRYOS.

Lukinovic describes the case of a patient who was operated on for a diagnosed ruptured ectopic pregnancy. Her last menstrual period started on April 3rd followed by attacks of pain on May 29th, May 30th, May 31st, and June 1st, after which laparotomy was carried out and the ovum which was lying free in the peritoneal cavity surrounded by blood-clot was easily identified and recovered. On opening the amniotic sac the embryo was found to measure 10 mm. and the longest diameter of the ovum was 20 to 22 mm. At the end of the operation it was noticed that distinct cardiac pulsation could be seen in the embryo at the rate of 74 beats per minute. For further observation the embryo was covered with warm normal saline solution and watched through a microscope. The cardiac pulsation continued for 30 minutes gradually becoming slower until it stopped.

The writer calculates that the age of the embryo was 47 to 50 days, or perhaps a little less, and points out that cardiac pulsation has been noticed in embryos measuring 6 to 6.5 mm. when these have been obtained by salpingectomy for an unruptured tubal pregnancy.

The interest of the writer's case is most marked in the recognition of the vitality of the foetus which permitted of cardiac pulsation for a period of definite length after the attachment of the ovum to the maternal tissues had been severed. The writer holds that the tubal abortion occurred 3 hours before the operation was begun and that this lasted 40 minutes, the embryonic heart beating for 30 more minutes, so that it survived for 4 hours and 10 minutes.

OLD MULTIPARAE.

Szolnoki, of the University of Budapest Second Gynaecological Clinic, reviews a series of 14,000 deliveries which occurred there during 5 years. The patients were divided into groups of 200 having had 2 to 6 deliveries and one group of 200 multiparae who had had 7 to 16 children.

He has drawn up various tables to give the percentage of abnormalities according to parity with the following results. Pregnancy toxaemia appeared in 3.16 per cent in women with 2, 3 and 4 children, and in 2.83 per cent in women with 5 or more children; retained products of conception in 2 per cent in the former group and in 4.16 per cent in the second; atonic bleeding in 3.83 per cent and 4.33 per cent respectively; placenta praevia in 0.66 per cent and 2.33 per cent; transverse lie in 1.33 per cent and 4.66 per cent; and early rupture of membranes in 11.33 per cent and 13.5 per cent.

The maternal mortality rose from nil in women with 2 or 3 children to 1 per cent in those with 4, 0.5 per cent in those with 5, and 1 per cent each for those with 6 and 7. The writer draws the conclusion that childbirth is safer for the mother up to the birth of her fourth child, especially if she is below 30 years of age. If her child-bearing is spaced to long intervals so that her first four children are not born before she is 30 years old then the added risk of her increasing age must be considered.

R. H. B. Adamson.

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Autotransplantation of the ovary. T. G. Knudtzon.

The excretion of gonadotropic hormone in the urine after ovarian transplantation in women. B. Heiberg.

The use of lumbar anaesthesia in induced abortion. E. Petersen.

Study of the state of blood-pressure during pregnancy, especially with regard to the connexion between hypertension and pregnancy toxicoses. E. Nordlander.

The action of oestrin upon corpus luteum function. A. Westman and D Jacobsohn.

*Experiments into the action of gonadotropic anterior pituitary hormones, antex (Leo), upon the ovaries. A. Westman.

Theca cell tumours, with reference to a case. S. Hammar.

EXPERIMENTS INTO THE ACTION OF GONADOTROPIC ANTERIOR PITUITARY HORMONES, ANTEX (LEO), UPON THE OVARIES.

Westman has observed the effect of antex (Leo) on human ovaries.

Patients who were to have laparotomy performed were given a course of premedication with antex in relatively large doses (9,000 to 10,000 me.). Later their ovaries were histologically examined.

The material obtained was divided into two groups. (1) Cases with healthy genitalia in which sterilization was carried out for psychosis, etc. (2) Cases of myoma.

(1) There were 7 cases in the first group. Three patients were operated on during a normal menstrual cycle, 1 pregnancy with induced abortion and 3 early during the puerperium. All cases showed a strongly increased follicular growth. Under normal conditions follicular maturation is inhibited during pregnancy and the puerperium.

(2) There were 7 cases of myoma, of which 5 showed strong follicular growth. No effect was observed in 1 case treated with weaker doses. The last cases were treated both with antex and with physex (Leo) (chorionic hormone) and it showed 3 fresh corpora lutea.

The effect of antex on human ovaries strongly resembles the one found in ovaries of the ape. All the ovaries investigated were capable of function. Whether similar results would follow the treatment of ovaries with pathological conditions, as in primary and secondary amenorrhoea, is now being investigated.

R. H. B. Adamson.

REPORTS OF SOCIETIES

ROYAL SOCIETY OF MEDICINE

(Section of Obstetrics and Gynaecology)

A Meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine was held on February 18th, 1938, when a discussion took place on

The Medical Aspects of the Decline of the Population.

The discussion was opened by Professor A. M. Carr-Saunders, who said that fertility has, in varying degrees, declined in nearly all civilized countries during the last 75 years. The causes of this movement are multiple and operate in various combinations in different countries, different areas of the same country, and in different social groupings. In a wide context of economic, social and psychological deterrents from parenthood, medical factors play a part. These fall into three main groups, which will be discussed by subsequent speakers:

(1) Sterility in men and infecundity in women give rise to the *incapacity* to conceive. So does impotence in men and the analogous conditions in women which prevent consummation of marriage.

(2) Various degrees of ill-health give rise to disinclination to conceive or a fear of conception, whereby fertility may be reduced.

(3) Various abnormalities may cause miscarriages.

Statistics of Childless Marriages.

Dr. R. R. Kuczynski said that the proportion of wives marrying under 30 years of age who remained childless, can be estimated for those who married in England between 1896 and 1901 at 8 per cent, for those who married in Norway between 1921 and 1924 at 8 per cent, and for those who married in Germany between 1924 and 1926 at 16 per cent. Assuming that in each case the proportion of involuntarily childless wives was 5 per cent, the proportion of voluntarily childless women among the fecund women who married under 30 years of age would have been about 3 per cent for England and Norway and about 12 per cent for Germany. In

France the proportion of childless marriages seems to be about as low as in Norway, while in Austria it is apparently much higher than in Germany.

Whether in England the proportion of wives marrying under 30 years of age who remain childless is now still 8 per cent or 16 per cent, or, maybe, 24 per cent it is impossible to say. It would also be a mistake to think that a few years hence, when the first statistics based on the records obtained under the new Population (Statistics) Bill will be available, we shall know much more about childlessness in this country. These statistics will tell us a great deal about the births which occur, but very little about the births which do not occur. They must be supplemented by triennial or quinquennial fertility censuses, the first of which ought to be taken within a year.

Medical Causes of Inherent Sterility and their Relative Importance.

Mr. EARDLEY HOLLAND spoke of the factors which influence the birth-rate; inherent or involuntary sterility is usually regarded as being a minor one, and of more consequence to individual couples than to the race. With this view he did not agree.

When 100 human couples, young and healthy, marry and have regular intercourse without the use of contraceptives, the results may be predicted somewhat as follows.

In a minority of cases pregnancy will occur immediately, the wife missing her first period. In the majority, pregnancy will occur after a variable period of delay, from a month to a year. In a few, pregnancy may be delayed for a still longer period, up to many years.

About 10 of the couples will remain childless. *Absolute fertility* means physiological perfection of the mechanism of conception. This state is common in animals, though by no means common in domestic animals or in captive wild animals. Human beings are, in comparison with animals, poor breeders; they are relatively, not absolutely, fertile. It has been said that most human couples who succeed in reproducing do so in spite of certain imperfections in the mechanism of conception.

In matings of high fertility pregnancy occurs promptly and repeatedly, often in spite of contraceptive precautions, and large families result. If the fertility of a mating is average, a desired pregnancy can usually be accomplished within a reasonable time, and an undesired one can be prevented with a fair amount of certainty. A mating of low fertility yields at most one or two pregnancies, often with long intervals of delay. This conception of relative sterility or relative fertility as applied to human matings is comparatively new and has done much to clarify the whole subject of human infertility.

The causation of inherent infertility. The right approach to the understanding of the problem of infertile marriage has come into being only during the past few years. In the past it was assumed that childlessness was due to the existence of a single causative factor, generally in the female, and once this factor was discovered, investigation stopped. Now, however, we recognize the existence of a whole collection of what are called infertility factors, some of which are of major and some of minor

importance. An investigation of a childless marriage, therefore, entails an exhaustive examination not only of each partner, but of the sum total of infertility factors found in both. The usual problem is not that of one definitely sterile partner mated with one who is unqualifiedly fertile, but rather that of two individuals of whom both exhibit some degree of infertility.

As an example of this a series of 100 cases of sterility investigated by Meaker may be cited. He found in these 100 cases a total of 481 infertility factors, of which 161 were male and 320 were female, the average number of factors per case being 4.81.

As regards the division of responsibility between the male and female, this is difficult to reckon with accuracy. All such estimates would be essentially fallacious, for they would be based on the erroneous idea that sterility is due to some single cause, which can be definitely allocated to one or other partner, whereas we know that most cases result from a summation of several causative factors. In Meaker's figures quoted above about one-third of the factors were on the male and about two-thirds on the female side. Thus the aggregate responsibility of wives appears to be greater.

Male factors. Nowadays, examination of the semen for the number and morphology of the spermatozoa is part of the routine investigation of all cases. It is stated, with more or less truth, that the minimal standard of male fertility is 60 millions per c.c., with not more than 30 per cent of deformed cells. All that can be said is that in about 40 per cent of sterile marriages the semen shows obvious defects in these respects—though such findings are no justification for fixing the blame exclusively on the husband, since in the same cases most of the wives also show infertility factors. Deficiency or absence of spermatozoa may result from two conditions: (1) defective spermatogenesis, due to what may be called depressed constitutional states; (2) the existence of a blockage in the ejaculatory ducts, or vasa deferentia, or somewhere else in the genital tract. The point to emphasize is that defective spermatogenesis is far the more important and more frequent of the two. In other words, the constitutional factors in the male preponderate over the local factors. As will be mentioned later, the same important generalization can be made concerning the female infertility factors—those due to constitutional or general causes preponderating over those due to local causes. Amongst the constitutional factors in male sterility may be mentioned pituitary malfunction, thyroid malfunction. chronic infection of the teeth or tonsils, malnutrition, alcoholism.

Female factors. These may be divided, like the male factors, into constitutional and local. Of the local factors I believe that far too much importance has been attached to tubal occlusion. This, as is well known, is a sequel of tubal infection—gonorrhoea, post-abortum or post-partum infection, or tuberculosis. Rubin, who introduced the method of tubal insufflation, states that he found some interference with tubal patency in 57 per cent of sterile women, and Meaker found obstruction or occlusion in about 25 per cent of his cases. Mr. Holland's experience is different, the

occlusion figure being 10 per cent in the last 100 cases subjected to lipiodol injection. In a certain pecrentage of cases tubal occlusion is only part of a genital hypoplasia, and should be reckoned as a constitutional and not as a local factor. That is to say, as failure of complete development of the reproductive system. In Mr. Holland's opinion this is by far the commonest cause of female sterility.

It is a common estimate that 30 or 40 per cent of all sterile women show stigmata of genital hypoplasia. The outstanding signs of this state are alterations in the size, shape and position of the uterus; actual measurement of the cavity is often of importance in establishing the diagnosis, and especially alteration in the right proportion between the uterine body and the cervix. Late onset of menstruation and irregularities of the function of menstruation are usual, but by no means invariable in slight cases. Uterine hypoplasia is no doubt an accompaniment of ovarian hypoplasia, with defects in follicles and hormones.

Genital hypoplasia being the most important female factor, the question naturally follows—what is its cause? Physiology teaches that ovarian function is chiefly dependent on the gonadotropic anterior pituitary hormones.

The tragedy about female genital hypoplasia is that medical advice about it is sought too late in life. The rule should be that if a girl does not menstruate regularly and normally before her fifteenth birthday, her general health and endocrine functions should be investigated. If the delay extends to her sixteenth birthday, the matter is really urgent. Even at this age it is doubtful if the necessary hormones and dietetic stimuli can be successfully given. The aim should be to try to detect the candidates for genital hypoplasia even before they reach the age of puberty. Is this possible? If hypoplasia could be anticipated early enough in life, there might be a chance of preventing it, and if we could prevent it the fertility of women would be remarkably raised.

To sum up, by far the most important *male* factor in sterility is defective spermatogenesis. By far the most important *female* factor is the corresponding one, genital hypoplasia. Both these are due to depressed constitutional states, the chief of which are defective endocrine action, especially of the anterior pituitary and thyroid glands, and chronic intoxications.

The connexion between hormones and vitamins is now being proved. The discovery that vitamins E and B are important for anterior pituitary function is significant, and suggests a nutritional basis for infertility.

Medical and Eugenic Deterrents.

Dr. C. P. BLACKER said that medical and eugenic deterrents from parenthood among many others operate to-day. Medical deterrents range from serious degrees of ill-health by which, if pregnancy occurred, life would be endangered, to minor ailments. Of these, the woman may feel that she does not want to run the risk of their being aggravated by another pregnancy. These minor degrees of ill-health rarely consitute the only reason or even the main reason why women do not wish to have more children; nevertheless they may play a subsidiary part which should not be overlooked.

Eugenic deterrents, while on the whole much less important than medical, appear to be increasing in frequency. Anxiety-states, occurring in married women, are frequently focused upon hereditary abnormalities in their families or their husbands' families, thus conducing to the limitation of families. There appears to be a risk that the fertility of socially valuable families may be reduced by an excess of misplaced eugenic zeal.

Changes in the Character of the National Diet during the past 250 Years and the Consequent Possibility of B and E. Shortage.

Professor J. C. DRUMMOND said that there has been a number of striking changes in the character of the English diet during the past 250 years, some of which have had a pronounced influence on nutrition. Of these none is more important than the change over from wholemeal to white bread, which occurred very rapidly about 1870 as a result of the introduction of the roller mill. The removal of the germ which the new process made possible brought about in less than 30 years a sharp fall in the amounts of vitamins B and E in the everyday diet of the people. For example, the intake of a poor person living largely on bread fell from about 800 international units daily to about 250. These two vitamins are very much concerned with the reproductive cycle, and it is possible that the introduction of white, germ-free breads has been in part responsible for lowered fertility.

The Part Played by Abortion.

Professor J. YOUNG stated that abortion and contraception are generally believed to constitute the effective influences in the declining birth-rate. It is impossible to determine the exact extent to which abortion operates in the absence of knowledge of the total number of pregnancies which so end prematurely. In a survey of gynaecological cases Beckwith Whitehouse found a history of 1,972 abortions in 11,430 pregnancies, that is 17.2 per cent. This estimate, however, is overweighted by the nature of the clinical material. In a survey of the reproductive history of 365 women in a medical unit there were 137 abortions in 1,265 pregnancies, or 10.8 per cent. These figures indicate that somewhere between 10 and 17 per cent of all pregnancies end in abortion.

From the medical standpoint abortion is sharply divided into two separate and distinct entities, (*a*) criminal or intentional abortion, and (*b*) spontaneous or pathological abortion. We have no accurate data regarding the relative proportion of these two conditions.

The Present Trend of the Population.

Sir LEONARD HILL said that according to Dr. Leybourne, the number of children in England will drop by four million, between the years 1931 and 1951, that is to say, from 9½ to 5½ millions. Even if this figure is reduced to 3 millions, it is alarming with regard to the future of our country.

During the same period the workers under 45 will have dropped one million, while all over 45 will have increased by 2½ millions. The drop

in youth and the increase in the aged must inevitably cause profound economic disturbance, and this will have to be faced durmg the next 15 years. The diminution in the supply of young people will affect all trades, all schools and all training colleges. There is already a shortage in the supply of domestic servants, who will cease to exist.

We have devoted efforts to prevent death and done nothing towards producing life.

Heavy taxes have been imposed in order to arm the country against possible enemies, while birth control is sapping the nation's power. The Press horrify us with statements concerning 7,000 deaths a year, on the roads, but are silent to the loss of 150,000 children a year by the fall in the birth-rate. A fall which is 50 per cent heavier among the intelligentsia than in the rest of the nation. Rates and taxes have gone up by leaps and bounds. The Government is spending 180 million pounds on public services. Habituated to a higher standard of comfort and heavily taxed, people have no money left for the begetting and nurture of children. The nation in truth has gone mad over expenditure. Some 350 million pounds a year are spent on motoring; the estimate for new roads is 81 million pounds. Millions have been spent on cinemas, on new public offices, on the development of seaside and other pleasure resorts. A new suburban council school has cost £40,000, and by 1951 there will be 4 millions less children in England and Wales. Like the Gadarene swine, the nation is running down a steep slope into the sea.

Schools and training colleges are already showing empty places. Colliery owners are offering free bicycles to tempt young men to become miners. Are Chinamen to be hired to work in our mines and in heavy occupations, and mercenaries to defend us?

The Democracies, Great Britain, France, Sweden, Norway, Austria, Czechoslovakia, Australia, New Zealand and the U.S.A., all have birth-rates below maintenance level, viz., 14 to 17. On the other hand, Germany has recently raised her birth-rate from 15 to 19. Italy stands at about 23. Japan numbers 70 millions, and increases by about a million a year. Russia expects to increase from 150 to 250 millions in 20 years. India, under our rule, has increased by some 40 millions in 10 years, and numbers 400 millions. The Boers increase in South Africa much faster than the British, as do the French Canadians in Canada. The birth-rate must conquer in the end.

Our profession should urge the Government to apply at once the methods used with success in Germany, there should be dowries for marriage and bonuses for children and family allowances in wages and taxes. Crèches should be provided where children can be placed while mothers are busy. All disabilities of illegitimacy should be removed; a woman has a natural right to bear a child, and the term "unmarried" should not be a necessary condition of employment. The begetting of children should be encouraged by propaganda as a national duty. Only by such means can the British Empire survive. The writing has appeared on the wall, and in the distance the vultures are gathering ready to sweep on a dying England.

Questionnaire with Regard to Children.

Dr. COOPER said that he had questioned 300 women in various hospitals, in filling up the questionnaire issued by the Population Investigation Committee. These questions were well devised and designed to throw light on the reproductive history of women and upon their attitude to child-bearing. He had not fully analysed the replies, but his impression at the moment that the greatest reason to be found for the determination to have fewer children was the parents' wish to do the best they could for their children and give them a good start in life, and this could be better effected by having few rather than many children. There was no evidence that the mothers of this generation were selfish or that they were determined to have a good time rather than bear children.

Birth control was certainly widespread in all classes, but he was surprised to find that there were so many, besides Roman Catholics, who were against birth control methods for all sorts of reasons. The use of birth-control methods may be a cause for part of the fall in the birth-rate, but it was well to remember that it was only a means to an end, and it was necessary to find out why they were used at all.

Inferences from the Reproduction of Fruit Flies.

Dr. MCCLEARY said that in seeking the causes of declining fertility attention should not be confined to this country. Fertility had begun to go down in different countries at widely differing times; in France over 140 years ago, in Japan about 10 years ago.

It had been suggested that when populations reach a certain density biological factors come into action limiting further increase, as was shown by the behaviour of fruit flies reared in bottles of known cubic capacity. This would not, however, explain the low fertility of Australia and New Zealand, both very sparsely populated countries, where the reproduction rate was now below the replacement rate. Decline in fertility had also been attributed to defective housing, but in the two dominions named housing conditions were greatly superior to those in this country.

The PRESIDENT of the Section, commenting on the speakers' remarks, agreed that economic factors were mainly responsible for the fall in the birth-rate. He was impressed by the fact that in his private practice, during the last 31 years, the percentage of women consulting him for sterility had risen, decade by decade, from 0.2 per cent to 6.6 per cent in the last 150 cases. There might be several explanations of such a rise, but he was chiefly impressed by the increasing number of instances in which two or more years of failure to conceive had been preceded by two or more years of the use of contraceptive measures. He thought that interference with the act of intercourse in early married life, especially in women already the subjects of some degree of genital hypoplasia, was inimical to fertility. He had been distressed to read in *The Times*, of all journals, the report of a suggestion that young women should be instructed in the use of contraceptive measures before marriage, in order that they might have more time to learn housekeeping and other wifely dutes during the first years of marriage.

He had learned that one economic factor in restricting the size of the family was the increased cost of institutional confinement as opposed to domiciliary confinement. The advantages of institutional confinement appealed to so many members of the professional and middle classes whose offspring should be of great value to the State, and therefore something should be done to lessen the cost.

The following also took part in the discussion: Mr. Wyatt, Dr. Dunlop, Dr. Alabaster, Dr. Brydone, Mr. Bourne, Mr. Lloyd, Dr. Wiesner, and Dr. Brend.

THE NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

NOVEMBER 1937

A meeting of the Society was held in Liverpool on 26th November 1937.

BRYAN WILLIAMS, M.D., M.C.O.G., F.R.C.S.E., read a paper entitled

FURTHER NOTE ON THE USE OF PRONTOSIL IN OBSTETRICS.

Mr. Williams said that the work he had reported to the Society in June had been continued, and on the whole the results given then had been supported. Since then, however, relatively few cases of haemolytic streptococcal infection had been available for treatment, till recently, when several patients had been admitted; but it was still too early to report the results in most of these. As the work had been continued on similar lines, details would not be given. The intramuscular route for giving the soluble prontosil, however, had been almost completely given up in favour of the oral route, the sulphanilamide preparation used being prontosil album. The intramuscular route, however, still had advantages in some cases, such as when a patient was very ill or was vomiting and could not swallow large numbers of tablets by mouth. Cyanosis also seemed to be a less prominent feature after injection of the soluble preparation.

Treatment. Altogether 84 cases had been treated and the results were shown in Table 7. Cases of established breast abscess and obvious pyelitis had been excluded.

In 44 cases a haemolytic streptococcus was not found. These would not be further discussed. No definite evidence had been found that prontosil was of value in these cases.

In addition, although large numbers of cases of pyelitis, either during pregnancy or the puerperium, had not so far been treated with these drugs, he had not found them to be of value in cases in which other treatment had failed.

In 40 cases a haemolytic streptococcus was isolated. A few cases of very mild infection in which the temperature fell before the organism was isolated had been excluded. It would be seen that in 29 of these, the infection was localized to the pelvis, and there were no deaths among these. In only two cases in Group 1 did the infection spread beyond the uterus. In one of these the condition subsided and the other patient went out against advice. In Group 2, however, there was a bigger tendency for an inflammatory mass to appear in the pelvis. In no case treated by prontosil from the beginning, however, had a mass appeared which failed to subside or which required incision.

In Group 3 there were 11 cases with 6 deaths. In five of these 6 it was previously reported that either the patient was extremely ill on admission or that treatment was commenced late or with what we now know to be inadequate doses.

It would thus be seen that as no further deaths had occurred since the last report, the mortality in all groups was somewhat reduced.

Eleven cases of mastitis had been treated. Abscess formation occurred in only 2, and in both of these the infection had commenced before labour and some time before treatment was commenced.

Prophylaxis. The results of the prophylatic experiment in cases having had major obstetrical interference were shown in Table 8, and the organisms found in Table 9.

Cases in which undesirable toxic effects might have appeared, such as toxaemia, being treated with magnesium sulphate, or cases of heart disease, were excluded, but otherwise, although the numbers in the treated and control series were unequal, no deliberate attempt was made to select cases.

It would be seen that there was little difference in the incidence or cause of the infection in the two series, except that mastitis was slightly less frequent in the prontosil series. Neonatal deaths were higher in the prontosil series, but there were none which could not be satisfactorily explained by the usual causes or could be attributed to prontosil. A few cases of neonatal sepsis, in the form of pneumonia, pemphigus, and gastro-enteritis, had occurred in both groups.

The important difference, however, between the two groups is that in the prontosil group, no cases of haemolytic streptococcal infection were found, although swabs were taken in 104 cases, whereas in the control series, among 73 patients swabbed, a haemolytic streptococcus was found 8 times. This controlled experiment, carried over a period of a year and including the great majority of the abnormal cases treated in that time, seemed to indicate very definitely that prontosil had a definitely protective effect against the haemolytic streptococcus in abnormal labour.

In addition, 4 cases in which an active haemolytic streptococcal infection had been present when labour or abortion occurred had been treated prophylactically, as shown in Table 10, and only 1 of these was slightly febrile for 1 day.

Toxic Effects. In speaking of the toxic effects Mr. Williams said that by now a long list was available of toxic effects which had been attributed to these drugs, the more important being jaundice, acute haemolytic anaemia, agranulocytic anaemia, cutaneous eruptions, and neuritis. Cyanosis had been a prominent feature, and had been found in 20 per cent of the prophylactic cases. It had seldom been persistent or accompanied by symptoms, and in the more serious of the infected cases the administration of the drug had sometimes been continued in spite of its presence. Otherwise, apart from skin eruptions and fever, he had noted none of the more serious effects, and altogether between 350 and 400 obstetrical cases in Walton Hospital had received the drug, in addition to many others which must now amount to several hundreds.

Discussion. Mr. Williams asked what was the place of these drugs in the treatment and prevention of puerperal sepsis? Most of the figures so far published, such as those in Table 11, showed that there had been a fall in the

mortality from haemolytic streptococcal infection since their introduction. At the same time there was some evidence that there had been a fall in the virulence of these infections in recent years—his experience at Walton Hospital certainly supported this view—though this could not explain the sudden fall which seemed to have occurred, as Gibberd had pointed out. There could, however, be no question that the use of these drugs in adequate doses in cases of haemolytic streptococcal infections produced a fall in temperature and an improvement in the patient's signs and symptoms that was often dramatic, especially when the patient was seriously ill with peritonitis or septicaemia. In fact it might almost be taken as an axiom that if this improvement did not occur, then a haemolytic streptococcus was not responsible. There was no justification, however, for the indiscriminate use of these drugs in all cases of puerperal sepsis. One often found now that cases were sent into hospital in which an indefinite amount had been given, of which no mention had been made. In any patient, however, who was seriously ill with a puerperal infection, Mr. Williams thought it was justifiable and even desirable that treatment should be commenced empirically with large doses, once cultures had been made. If, then, the infection was found to be due to a haemolytic streptococcus, very valuable time would have been saved, and if not, no harm would have been done.

Perhaps the only way in which they could decide the problem would be to start all over again, and treat alternate cases with and without the drugs; but he thought no one would have the courage at the present moment to do it.

What was their use in prophylaxis? Evidence had been brought forward to show that they had a protective effect against the haemolytic streptococcus in abnormal labour. There was, of course, no reason why cases of abnormal labour should become infected with the haemolytic streptococcus any more than normal cases; if anything, as Colebrook had suggested, the risk was less, owing to the more strict antiseptic technique used. It seemed reasonable, however, to assume that the same findings could be applied to normal labour.

The main question to be decided was whether their routine was justified in either normal or abnormal labour. The risk of a patient's contracting a haemolytic streptococcal infection in ordinary circumstances was slight. Dr. Dora Colebrook, in 1935, had given figures showing the incidence of such infection at three separate institutions to be 1 in 400, 1 in 1,000, and 1 in 1,900 respectively. Hare and Lancefield, in 1935, had found that haemolytic streptococci could be isolated in as many as 10 per cent of cases in the puerperium, in only 1 out of over 800 cases in the puerperium was a serious haemolytic streptococcal infection found. In the present series a haemolytic streptococcus was found only in 8 cases out of the 311 control cases, though, of course, swabs had been taken only in febrile cases, and in most of these the infection was a mild one. It would seem, therfore, that at present the risk of a patient's becoming infected with a haemolytic streptococcus in ordinary circumstances was infinitely less than the risk of cyanosis occurring with the routine use of the drugs. It did not seem justifiable, therefore, to use these drugs as a routine in either normal or abnormal labour, and he had discontinued this practice now that the experimental work had been carried out.

Mr. Williams said their main use, as pointed out by Colebrook, in 1937, for prophylaxis, was in cases in which the patient was suffering from a haemolytic streptococcal infection at the time of delivery or abortion, and 4 such cases had been described, or in cases in which the attendant or someone in the neighbourhood had harboured a haemolytic streptococcus at the time of delivery.

It had now been proved beyond all doubt that the source of virulent haemolytic streptococci in puerperal sepsis was either a septic focus in the neighbourhood, or the respiratory tract of an attendant. We seemed to have a powerful weapon in the prevention of such infection. This was the kind of infection that provided most of the serious cases and the epidemics, that in the past had proved so capricious, and in the present seemed so often to lead to law-courts. The results in this direction gave us hope that we might also be successful in the treatment of infections due to other organisms with the newer drugs now becoming available.

Discussion. Dr. HERD (Liverpool) said that he had sometimes found that cases which do not respond at first to prontosil do so after a blood transfusion.

Professor JOHN CHISHOLM (Sheffield) said that the drugs had been used a great deal at the Jessop Hospital and the results had been comparable with Mr. Williams's.

Mr. A. GEMMELL (Liverpool) quoted a case in which pyrexia was due to prontosil; when the drug was discotinued the temperature fell.

Mr. C. WALSH (Liverpool) thought it probable that some people had an idiosyncracy to prontosil.

Mr. BURNS (Liverpool) had seen a case in which cyanosis persisted for a month.

Mr. JEFFCOATE (Liverpool) thought that cyanosis depended on the patient and not on the dosage. He had seen cases of pyrexia and jaundice following its use.

In reply, Mr. Williams said blood transfusion had been carried out in many cases with marked improvement. The dosage he gave was 4 tablets of 0.5 gramme 4-hourly. After a few days he reduced the dose to two-thirds. He thought that cyanosis might be due to an idiosyncracy. He had not yet worked out a diet containing the minimum of sulphur.

TABLE VII.

Results of treatment with prontosil.
Cases in which a haemolytic streptococcus was not isolated.
44 cases 3 deaths Mortality = 7 per cent.

	GROUP 1	GROUP 2	GROUP 3
	Infection localized to perineum, vagina, and uterus	Infection involving pelvic cellular tissue, peritoneum, veins, Fallopian tubes or ovaries	Septicaemia, or peritonitis, or both
Number of cases	19	10	11
Deaths	0	0	6

Total mortality	9 deaths in 84 cases = 11 per cent
Mortality of cases infected with haemolytic streptococci ...	6 deaths in 40 cases = 15 per cent
Mortality of septicaemia	6 deaths in 10 cases = 60 per cent
Mortality of puerperal septicaemia at Walton Hospital, during 1934, 1935, and 1936 (prior to the introduction of prontosil)	26 deaths in 30 cases = 87 per cent
Mortality of non-pelvic septicaemia during 1934, 1935, and 1936	23 deaths in 25 cases = 92 per cent

TABLE VIII.

Results of prophylaxis experiments.

	Prontosil cases	Control cases
Total	257	311
Death	1 (mitral stenosis)	0
Morbidity		
B.M.A. Standard ...	52 = 21 per cent	71 = 23 per cent
Public Health Standard	39 = 15 per cent	47 = 15 per cent
Infection of pelvic origin	28 = 11 per cent 1. Bacillus coli septicaemia 2. Streptococcus viridans septicaemia	32 = 10 per cent 1. Bacillus coli septicaemia 2. Staphylococcus aureus septicaemia 3. Pelvic peritonitis
Pyelitis	15 = 6 per cent	14 = 4 per cent
Mastitis	2 = 1 per cent	8 = 3 per cent (1 abscess)
Neonatal deaths ...	15 = 6 per cent	12 = 4 per cent
Cyanosis	51 = 20 per cent	—

TABLE IX.

Organisms isolated from lochial swabs.

	Prontosil cases	Control cases
Number of swabs	104	73
Haemolytic streptococci	0	8
Non-haemolytic streptococci ...	5	5
Staphylococcus aureus	15	6
Bacillus coli	34	32

TABLE X.

Mastitis.

Total number of cases treated, 11. All of these subsided, except two, in which abscess formation occurred. In both of these, the inflammation had commenced before delivery.

HAEMOLYTIC STREPTOCOCCAL INFECTION COMPLICATING PREGNANCY (4 CASES).

1. Quinsy ...	Haemolytic streptococci present in throat	Inevitable abortion	Non-febrile after first day
2. Quinsy ...	—	Complete abortion	Non-febrile
3. Tonsillitis; contact scarlet fever ...	Haemolytic streptococci present in throat	Normal labour	Non-febrile
4. Erysipelas ...	—	Inevitable abortion	Non-febrile

TABLE XI.

Results reported with prontosil in puerperal sepsis.

	All cases		All haemolytic streptococcal infections		Septicaemia due to the haemolytic streptococcus	
	Pre-prontosil	Prontosil	Pre-prontosil	Prontosil	Pre-prontosil	Prontosil
Gibberd (London) 1937	—	—	210 cases, 20 per cent mortality	157 cases, 4.5 per cent mortality	28 cases, 40 per cent mortality	21 cases, 20 per cent mortality
Foulis and Barr (Glasgow) 1937	1,988 cases, 13.5 per cent mortality	70 cases, 1.4 per cent mortality	—	18 cases, ? 6 per cent mortality	—	8 cases, ? 12½ per cent mortality
Brown (Belfast) 1937	—	—	23.5 per cent mortality	6.6 per cent mortality	87.5 per cent mortality	28.6 per cent mortality
Williams (Liverpool) 1937	—	84 cases, 11 per cent mortality	—	40 cases, 15 per cent mortality	30 cases, 87 per cent mortality	10 cases, 60 per cent mortality

The President, Dr. BRIDE read

A FURTHER REPORT ON A CASE OF MALIGNANT TUMOUR OF OVARY AND LUNG IN A GIRL OF TWELVE.

Dr. Bride said that on February 26th, at the Liverpool meeting of the Society, he had shown a specimen of malignant tumour of ovary and lung in a girl of 12.

He had described it as a mixed-celled type of sarcoma of the ovary with secondary deposits in the lung.

He had discussed the differential diagnosis with respect to malignant teratoma and chorion-epithelioma. Since then he had sent sections of the ovary and lung to members of the constituent centres and had received replies from the following: Professors Phillips and Dougal, who both considered the tumours to be malignant teratomata. Mr. Jeffcoate had said in a letter to him, "Personally I think the tumour a very malignant teratoma since it appears to contain both epiblastic and mesoblastic tissues ".

Dr. Bride thought that the Society would agree, therfore, that the specimen could now be described as one of malignant teratoma of ovary and lung.

Mr. C. J. K. HAMILTON (Liverpool) described

A CASE OF ACUTE YELLOW ATROPHY.

He said the patient, B. J. C., had 1 child and was aged 32. She was admitted on the 10th August 1937 during the evening. She was sent in by her doctor as a case of cardiac disease.

Her previous pregnancy had been normal and she had had a normal delivery on the 27th May 1935 of a full-time child which, however, had a spina bifida.

Her last menstrual period had been on November 30th, 1936. She had been perfectly well until one week before admission. During that week she had had attacks of orthopnoea, and with these attacks she was said to become blue. She had also had anorexia, but had only vomited three times. There was no history of any drugs having been taken.

The relatives had noticed some drowsiness for the two days prior to admission.

On admission the temperature and respiration were normal, but the pulse-rate was 120. The next day when seen by Mr. Hamilton in the daylight she was seen to be slightly jaundiced.

The pulse-rate was 120, respiration 28, and temperature normal. Breathing was rather laboured and she was drowsy; it was, therefore, impossible to obtain the history.

Examination of the heart, chest, and central nervous system showed no abnormality. On examining the abdomen the uterus corresponded in size to the period of pregnancy—36 weeks.

The vertex was presenting, the foetal heart sounds were heard. The liver and spleen were palpable; percussion of the liver revealed some apparent diminution of dullness.

Classical Caesarean section was performed under local anaesthesia, and a living male child weighing 6 pounds 10 ounces was delivered. Saline containing 10 per cent of glucose was given by the drip method with 10 units of insulin in each pint. The next day the abdomen was slightly distended and the hepatic dullness seemed to be more diminished. The jaundice was more marked, but there was no vomiting. The temperature was 100°F. and pulse-rate 110; the pulse was of better volume than the previous day. Ten cubic centimetres of a 10 per cent solution of calcium gluconate were added to to the saline on two occasions, and 25 ounces of urine were passed.

The next day the jaundice had become still deeper and the patient was nearly comatose. The liver dullness appeared to be completely absent. No twitching was observed. The temperature had risen to 104°F., the patient had two rigors; 91 ounces of urine were passed.

On the morning of 14th August the patient died.

The infant was noticed to be slightly jaundiced the day after operation and the jaundice appeared to be increasing. Paternal blood, and later serum, was given for the ensuing 4 days, and the jaundice gradually cleared.

Mr. Hamilton said that he had seen the child 2 days before the meeting; it was then gaining weight, and was apparently very fit, weighing 10 pounds 11 ounces.

At the maternal post-mortem the liver and spleen were not palpable. All the organs were normal except the liver and kidneys.

The liver weighed 40 ounces; the capsule was yellowish in colour and not wrinkled.

On cut section red areas of necrosis surrounded by paler areas of fatty degeneration were seen; the gall bladder was normal and the ducts were patent.

The right kidney showed some hydronephrosis; the left pyelitis.

Microscopically there was necrosis and fatty infiltration of many of the hepatic cells in the central areas. The lack of gross pathological changes was, he supposed, due to the acuteness of the condition.

The question of the jaundice of the child was interesting. There were few references in the literature to the infant, but Dudley in 1901 had reported a case with normal delivery in which the child was born jaundiced.

Discussion. Dr. N. B. CAPON (Liverpool) referred to the relation between icterus gravis, anaemia gravis, and congenital oedema of the foetus; and said that cases seen in this country seemed to show erythroblastosis much less frequently than those recorded in America.

Early treatment by the intramuscular injection of human serum was of the greatest importance, and maternity hospitals should keep a supply of serum available for use in emergency. As soon as the child was out of danger and the jaundice was subsiding, blood transfusions were of value to overcome the consequent anaemia.

Mr. C. H. WALSH (Liverpool) reported a case he had seen at the same time as Dr. Hamilton. The patient was admitted at the twenty-fourth week of pregnancy, with right-sided pain and vomiting for the previous 5 days. There was slight jaundice, but her condition was fair. At a previous pregnancy she had jaundice 7 weeks after delivery, but this had cleared up in a few days. The urine contained pus and bacilli coli.

She was treated with calcium gluconate and glucose, and the membranes were ruptured to induce abortion. She was delivered on the following day and died two days later. A post-mortem showed typical necrosis of the liver.

Mr. Walsh suggested that this was a case of toxaemia in which the toxin primarily affected the liver, with no damage to the kidneys.

Toxic jaundice might be a terminal disease in some cases of severe vomiting. He suggested that there might be specific toxin elaborated which had a selective destructive effect on the hepatic cells in toxic jaundice.

Professor A. M. CLAYE (Leeds) read a paper on

A CASE OF ENDOMETRIOSIS.

The patient, aged 30, had a menstrual cycle of 7/30 days with normal loss. She had complained of dysmenorrhoea for several years with recent exacerbation. She also complained of sterility, having been married 9 years without a pregnancy, and of internal dyspareunia. An indefinite mass was felt behind the uterus and there were no signs of gonorrhoeal infection in the lower genital tract. The husband had recently had gonorrhoea, but in spite of this a tentative diagnosis of endometriosis was made.

At operation in March 1936 the left ovary was found enlarged and bound down by adhesions. On separation of these a cyst in the ovary burst and chocolate material exuded. This ovary was removed. The right ovary was slightly enlarged and contained multiple cysts. A wedge was enucleated and the ovary sutured. The appendix was removed. Clinically this was a case of endometriosis though the pathologist did not commit herself absolutely. She said it was probably an old endometrial cyst, though there was nothing absolutely diagnostic. The cyst was lined by pigmented granulation tissue, common in endometrial cysts. The patient made a good recovery. The dyspareunia was relieved and the dysmenorrhoea was very much less marked. Professor Claye saw her again the day before the meeting, when she was about 32 weeks pregnant.

On rapid inspection of his hospital records he could find only two other examples of pregnancy following conservative operation for endometriosis, but as the cases had not been systematically followed up and he knew of these three, it appeared probable that pregnacy in these cases was not so rare as he had supposed. Briefly the other two cases were as follows:

Mrs. O'H. was aged 28; she had no children, but had had one miscarriage at the eighth week 17 months before. Her menstrual cycle was 5/30 days; the loss was not excessive and she did not have dysmenorrhoea. Her main symptom was pain in the right iliac fossa. Dyspareunia was marked.

At operation some small fibriods were removed. The left ovary and left Fallopian tube were removed with chocolate cysts; the right ovary was normal. The patient had a normal confinement just over a year later.

Mrs. K. G. was aged 26; she had been married one year and had no children or miscarriages. Her menstrual cycle was 5/28 days; the loss was normal; she had had dysmenorrhoea since the menarche, but it had been much worse during the previous six months. She had internal dyspareunia.

In June 1936 the cervix was dilated and the uterus curetted. There was endometriosis of the recto-vaginal septum confined histologically with a small nodule above it on the right side of the back of the uterus. No other evidence of endometriosis was found. A small piece was excised for biopsy, the appendix was removed and the abdomen was closed. This patient was seen about a month ago when she was 16 weeks pregnant.

He had met with endometriosis at Caesarean section on three occasions. It was confirmed histologically in two of them. All three operations were done for placenta praevia.

Bourne and Williams stated that nearly 50 per cent of patients with endometriosis are completely sterile. The explanation of this was not altogether clear. Perhaps it was an example of two associated kinds of ovarian malfunction. In some cases no doubt the fimbriated ends of the Fallopian tubes might be closed by adhesions, and in some cases the dyspareunia militated against conception.

Professor Claye said he was not in a position to dogmatize about the incidence of pregnancy in association with, or after conservative operation for endometriosis, but he would plead that in patients in whom the disease was not very advanced an attempt should be made to leave some ovarian tissue behind to preserve the possibility of pregnancy. If the symptoms returned they could be treated by means of X-rays. His impression was that the age period of this disease was put too high by most authorities. Bourne and Williams said 30 to 47. He had a good many cases below the age of 30.

Discussion. The PRESIDENT, Dr. Bride, and Professor MILES PHILLIPS (Sheffield) had each seen a case of endometriosis in which pregnancy had supervened.

Professor PHILLIPS thought that the artificial prevention of pregnancy in early marriage might possibly be the cause of endometriosis.

Mr. ST. GEORGE WILSON (Liverpool) was of opinion that many cases of chocolate cyst could not be demonstrated as endometriosis, and it was in these cases that pregnancy occurred.

Professor LEYLAND ROBINSON (Liverpool), Mr. JEFFCOATE (Liverpool), and Mr. A. A. Gemmell (Liverpool) had all seen cases similar to that of Professor Claye.

In reply, Professor CLAYE expressed the opinion that his case was one of true endometriosis. He thought that the incidence of sterility was exaggerated.

Mr. A. A. GEMMELL (Liverpool) showed a specimen of

CARCINOMA OF THE ISTHMUS UTERI.

Mr. Gemmell said that the patient from whom the uterus had been removed was a woman aged 35 years. She was nulliparous, married at the age of 32½ years, and had been a widow for almost a year. Her husband had died of rheumatic endocarditis.

She had had floodings 8 months and 7 months before she consulted him, and for 5 weeks prior to the consultation had felt "something in the passage."

On examination a small polypoid mass was palpable at the external os, and this bled so profusely, as the result of the examination, that the vagina had to be packed. She would not consent to operation until a month later.

When removal of the polypus was attempted, it was obvious that its pathological nature was unusual. Histological examination proved it to be a columnar-celled carcinoma. On this account, and as the uterus was fairly mobile, it was removed by Wertheim's hysterectomy on September 14th, 1937. Enlarged lymphatic glands were not found. The patient made an uninterrupted recovery. She was seen 3 weeks ago, and reported herself as feeling very well. The abdominal and vaginal scars were sound, whilst there was no thickening in the parametria.

The specimen shows a polypoid mass growing from the posterior wall of the cervical canal, just above the level of the internal os. As already stated, sections proved it to be an adenocarcinoma.

Discussion. Professor MILES PHILLIPS (Sheffield) said the prognosis in these cases was gloomy because the operator did a panhysterectomy, and not Wertheim's hysterectomy, in the belief that he was dealing with carcinoma corporis.

Professor DOUGAL (Manchester) said that if it could be recognized that the growth was low in the uterus Wertheim's operation should be done.

Mr. MALPAS (Liverpool) had seen a case which had done well under deep X-ray therapy.

Mr. GEMMELL showed a specimen of

SARCOMA OF THE UTERUS.

This specimen has been removed from a spinster aged 58 years. The menopause had occurred 10 years previously, and at that time there had been some flooding. There had not been any discharge or bleeding at all since the last menstrual period.

She had complained only that she had noticed a lump in the abdomen for the past month or two, four at the very most, that she had some frequency of micturition by night, and increasing constipation.

Examination showed a lobulated swelling occupying the lower abdomen, and reaching to about two fingers' breadths below the umbilicus in the centre, and a little above it on the right. The mass was mobile. Rectal examination revealed the lower pole in the right fornix, and it was thought to be independent of the uterus. A diagnosis of a multilocular ovarian cyst was made.

Under anaesthesia a thorough vaginal examination was carried out, and it then appeared that the mass was continuous with the cervix, and that the body of the uterus could not be identified apart from it. This examination did not provoke any bleeding.

When the abdomen was opened the appearance of the mass supported

the opinion which had now been formed, that the true diagnosis was sarcoma of the uterus. Total hysterectomy with removal of both appendages was carried out. There were no adhesions and no difficulty was encountered during the operation. The patient had an uneventful convalescence and left the hospital on the twentieth day. She might have left a few days earlier, but preferred to stay as there was not anyone to look after her at home.

Sections showed the tumour to be round-celled sarcoma with a few giant cells. Such sections as had been cut did not show any evidence of connexion between the tumour and the endometrium. This, coupled with the fact that the uterine cavity was hardly distorted, accounted for the absence of bleeding.

Mr. Gemmell said the sarcoma evidently arose in the vaginal wall. The general outline of the mass, and the fact that there were floodings at the time of the menopause, made him think that this might be a sarcomatous change in a fibroid or fibroids, but the limited sections which had been cut did not supply any evidence in support of this hypothesis.

Discussion. Professor MILES PHILLIPS (Sheffield) had operated on one such case 5 years ago. The patient was still alive.

Mr. ST. GEORGE WILSON (Liverpool) showed a cinematograph film entitled

A METHOD OF DELIVERING THE TRUNK AND ARMS IN BREECH PRESENTATION.

Mr. ST. GEORGE WILSON said that in the *Journal of Obstetrics and Gynaecology of the British Empire* published in August 1937, an article appeared entitled "Shoulder Delivery by Breech Presentation" by Jrgen Lvset, from the Maternity and Women's Hospital, Bergen.

In this article the writer discussed the classical methods of bringing down extended arms in those cases of breech presentation in which they were displaced, and described his own method.

The theory underlying this method was that the posterior shoulder was lower than the anterior owing to the inclination of the pelvis, and when the anterior shoulder stemmed behind the symphysis pubis, the point of the posterior shoulder was below the promontory of the sacrum.

If, and when, the posterior shoulder had come down to the level below the promontory of the sacrum, the body of the child was rotated through 180°, the posterior shoulder would come behind the symphysis pubis, and the arm would appear under the pubic arch In many cases it would fall out itself, but if not, it could easily be lifted out with a finger under the upper part of the pubic arch.

When this arm was free, the trunk was rotated back again through 180°, and the arm behind came to the front in its turn, and appeared under the pubic arch.

For this method he claimed that (1) it was easy, (2) displacement of the arms was an advantage rather than a hindrance, (3) the insertion of the

hand into the vagina was unnecessary, and the risk of laceration and sepsis was obviated.

Mr. St. George Wilson said he had tried it on the mannikin and in a few patients, and found that the method worked admirably, and he had shown two films in which the body and arms were delivered, in one case without touching the arms at all.

He would suggest that it was a good easy method to be taught to students and pupil midwives.

One word of warning he thought should be spoken: special care should be exercised in holding the body of the child during the turning movements, as damage to the abdominal viscera might result.

Discussion. Mr. BURNS (Liverpool), in discussing the method, thought it had nothing to recommend it. There was a risk of breaking the foetal neck by twisting.

Mr. MILES PHILLIPS (Sheffield), Mr. GEMMELL (Manchester), and Mr. GLYN DAVIES (Sheffield) all thought the method an excellent one, and had used it for years.

Mr. PHILLIPS pointed out that the method had been originally adopted by Potter, of Buffalo.

ROYAL ACADEMY OF MEDICINE IN IRELAND

JANUARY 1938

A meeting of the Section of Obstetrics of the Royal Academy of Medicine was held in the Royal College of Physicians on Friday, January 14th, 1938; the President, Dr. J. S. Quin, was in the chair.

Dr. CORBET showed slides and microphotographs, very kindly prepared by Dr. McGrath of St. Vincent's Hospital, of

AN EARLY KRUKENBERG TUMOUR.

The interesting features of the case were that the patient was aged 50 and had passed the menopause 2 years previously. She was admitted to the Coombe Hospital with an abdominal tumour which was diagnosed as an ovarian cyst. At laparatomy, this ovarian cyst was found to be about the size of a six months' pregnancy originating from the right ovary. The naked-eye appearance suggested malignancy. On inspection the left ovary was found to be about as large as a walnut, white and hard. This was also removed and it proved to be a Krukenberg tumour.

The large tumour was a simple cyst-adenoma. A series of X-ray photographs of the gastro-intestinal tract showed a picture diagnostic of advanced scirrhus carcinoma of the stomach.

The patient refused a second laparatomy and returned home to the country.

Discussion.—The PRESIDENT said that this case was unusual because the tumour of the ovary was so immature that the diagnosis on the microscopic appearance had proved very difficult even to the pathologist. Until recently the view had been held that these tumours were entirely metastatic. The other view, mentioned by Dr. Corbet, that a Krukenberg tumour was the reaction of the ovary either to the malignancy in the stomach, or to the cause of the malignancy in the stomach, was very attractive. But the exponents of this view had not so far given any reason why these tumours were associated only with gastric carcinoma, and not with carcinoma in any other part of the gastro-intestinal tract, or in the body elsewhere.

Dr. G. C. DOCKERAY referred to a specimen in the Rotunda Hospital of a Krukenberg tumour in which the primary growth had been in the breast.

Dr. Corbet, in replying, said Krukenberg tumours had been described in cases in which carcinoma was not present at all: they had been diagnosed in some cases in which the patients had survived for 10 years without any evidence of carcinoma.

The PRESIDENT read

NOTES OF A CASE OF ACUTE APPENDICITIS IN THE PUERPERIUM FOLLOWING CAESAREAN SECTION.

Dr. KEVIN FEENEY read

A NOTE ON OBSTETRIC SHOCK

Having reviewed the theories relative to the aetiology of shock in general, he indicated the procedures which are most likely to lead to shock in obstetrics. This latter type of shock is not difficult to understand and is in no way different from surgical shock.

He then considered the type of shock that is known as obstetric shock—the aetiology of which still remains in doubt. He discussed the clinical features of this type of shock and stressed the difficulty and importance of making a diagnosis between it and concealed haemorrhage, the possibility of uterine rupture should be especially borne in mind.

He referred to the difficulty which may arise in this type of shock when the placenta is retained but laid down no definite rule as to when it should be removed. He was of opinion that retention of the placenta may increase shock, but he offered no explanation as to how this happens.

He then reviewed the possible causes which predispose to shock and would seem to incline to the view that the hypochromic type of anaemia, so common in the hospital type of patient, has an important bearing. He illustrated this latter point in the case history of four pregnancies in the same woman observed at the Coombe Hospital. In each of her labours she suffered from severe obstetric shock. On the last three occasions a blood-count was done and showed the percentage of haemoglobin to be 30, 42 and 27 respectively.

He very fully reviewed the treatment of shock and issued a timely warning against over-treating these cases.

Discussion. Dr. KERRY REDDIN, in thanking Dr. Feeney for his paper, said he thought it was a very good thing that the subject of obstetric shock should be discussed. In his opinion most of these cases were due to malnutrition. Some of these women were in a low state of health from anaemia from this cause. He had felt for a long time that a large number of women were killed by shock on the district.

Dr. G. C. DOCKERAY said that Sir John Lumsden had asked him if he would, at intervals, estimate the haemoglobin of some of the women who attended the dinners given by the St. John's Ambulance Association. He had up to the present only done about 40 estimations, and the figures were just as bad as he would have imagined, from the appearance of the women. The worst degree of anaemia was 33 per cent; 50 to 60 per cent was fairly good, and only on one occasion had he got a figure of 90 per cent. Recognition of the anaemia was very important, and a special watch should be

kept for the rare cases of macrocytic anaemia. The pernicious anaemia of pregnancy also included the anaemia which might come on more rarely in the puerperium. He had seen about 10 cases of this. One woman had died, and at post-mortem a clot was found in the cerebral artery. He had recently had a very bad case of anaemia under his care in hospital. The woman was admitted in August. She had had twins the previous May. She came up from the country, and on admission her haemoglobin was only 10 per cent and her red-cell count was under half a million. She was suffering from incontinence of urine and faeces. A Van den Berg test was done and was a great help, because it showed that the case was of the haemolytic type of anaemia. The blood-picture was that of pernicious anaemia. She was put on large doses of campolon. She did not respond to this. A couple of days later she seemed to be much worse, and so was given a transfusion of 250 c.c. of blood. This was repeated three days later. During the next three weeks she had nine transfusions. After this she began to respond to the campolon, improved considerably, and left hospital with a blood-count of four million red-cells.

Apparently this patient's bone marrow was in such a bad condition that it would not respond to treatment, as it did in most cases. The giving of iron to women in the antenatal clinics could be increased with advantage. At present much was given at the antenatal clinic at the Rotunda Hospital, but more was necessary.

Dr. H. TIGHE said he was interested to note that Dr. Feeney had divided obstetric shock into shock which occurred after traumatic delivery, which could be readily understood, and shock which occurred for no obstetric reason whatever. He wondered why it was that some women could retain the placenta for an hour and a half or two hours and show no signs of shock, while others if they retained it for barely half an hour showed signs of collapse. It was difficult to understand how a woman who did not bleed became collapsed. The woman who suffered from ante-partum anaemia was really in the position of her robust sister who bled immediately after delivery. He wondered if this was due to the fact that the placenta was retained because the woman was not in such a condition as to be able to expel it herself.

Dr. R. M. CORBET congratulated Dr. Feeney on his excellent paper on obstetric shock. He said that the diagnosis between obstetrical shock and the shock caused by concealed haemorrhage, that is, intra-abdominal bleeding or retro-peritoneal bleeding from rupture of the uterus, was one which was very difficult to make. Yet, if the diagnosis was not made, the wrong treatment might be instituted and the result might be fatal. During the past year two fatalities had occurred in his service; one case in which the patient had died from haemorrhage from unsuspected rupture of the uterus when she had been treated for shock; and the other in which the patient had died from shock when an internal haemorrhage had been suspected and the treatment directed towards that end.

He thought that in cases of shock, care should be taken in introducing too much fluid into the blood-stream: that a possible feature of some of the cases was dilatation of the heart, because he had come across patients

whose pulse was extremely rapid and feeble, yet whose general condition was good, out of keeping with the pulse-rate, and who eventually completely recovered. He said he found it very difficult to make up his mind when he saw those patients at first in a condition of collapse, whether the uterus should be explored or not, and he felt that, when there was any uncertainty whether the uterus was ruptured the risk of exploration would have to be undertaken. He quite agreed that the majority of cases of shock occurred in undernourished and anaemic patients.

Dr. J. F. CUNNINGHAM said that Dr. Feeney had given a very lucid survey of the subject of obstetric shock. If a patient died from obstetric shock the death certificate should not be signed until a post-mortem examination had been carried out. In most of these cases some underlying clinical conditions would be found. In the National Maternity Hospital, of which he was Master, they had a large number of patients who required very careful handling and a great deal of care. Patients who had had even slight ante-partum haemorrhage became shocked very easily, even though labour had been fairly normal. There had been one or two cases of anaemia under his care which were so bad that he had given a blood transfusion and induced labour because they were not responding at all to treatment. The first thing to remember about the treatment of shock was not to overdo the treatment. These patients had to be handled very gently. He always gave morphia first of all, and if an anaesthetic was necessary he gave gas and oxygen. Glucose saline was better given subcutaneously than intravenously. If a blood transfusion was given, it was better to give it by the drip method. The bed should not be elevated unless the patient was delivered, as elevation of the bed would not improve her condition. After delivery it was a slight help to raise the foot of the bed 6 or 8 inches. He was of opinion that patients suffering from shock should not be given pituitrin. Half an hour after it was given the effect seemed to wear off, and he had found that patients did not like it.

The PRESIDENT said that Dr. Feeney had dealt with a very difficult subject in an exhaustive way. Dr. Fitzgibbon, to whom he was Assistant at the Rotunda Hospital, would never allow it to be said that obstetric shock existed, and said that these cases were due to haemorrhage. It was not, he thought, fair to call a condition in which a patient had lost only a small amount of blood at delivery, but had previously lost a great deal, obstetric shock. Obstetric shock had to be very carefully distinguished from haemorrhage, external or internal, and from rupture of the uterus. None of the cases which died should be diagnosed as obstetric shock without a post-mortem examination being carried out. Over-treatment of these cases was worse than no treatment at all. It was difficult to know what was the cause of the very profound shock which was found in cases of inversion of the uterus. There was no haemorrhage, and yet invariably there was a very profound degree of shock producing such a condition as absolutely to prevent further treatment. He asked Dr. Feeney if he thought that lack of calcium in the diet had any predisposing influence on this condition.

Dr. FEENEY, in replying, said that undoubtedly malnutrition was a very important factor in anaemia. The question of the onset of shock and

placental retention was, he thought, very largely a matter of the patient's general condition. Blood transfusion before labour, to tide the patient over labour, was a very good thing.

Dr. H. TIGHE read

A NOTE ON A FOURTH PREGNANCY IN A DIABETIC WOMAN.

This was an addition to a communication read to the Section last April entitled "Notes on three pregnancies in a diabetic," and which was subsequently published in the August number of *The Irish Medical Journal*.

The patient, Mrs. M.D., 27 years of age, first came under care three years ago. She had been married for 15 months, and was 4 months pregnant. She had been under rigorous treatment for diabetes mellitus for 5 years but had only been receiving a large amount of insulin during the previous 6 months. She had on one occasion been admitted to hospital in diabetic coma, and when first seen she was receiving 75 units of insulin per diem. Her first pregnancy ended at the thirty-second week. Her second pregnancy, beginning 5 months later, also ended at the thirty-second week. Both babies were small and survived for only 30 minutes. Her third pregnancy, which commenced 2 months after the second, proceeded to the thirty-seventh week, when labour was induced, on account of the large size of the baby. This child, weighing 6 pounds 10 ounces, lived for 2 days. At autopsy, death was found to be due to renal apoplexy.

This patient became pregnant for the fourth time last April, that is in April 1937, 4 months after her third pregnancy. She was confined last December at the thirty-fourth week and gave birth to a baby weighing 7 pounds, which now, when 16 days old, shows every sign of surviving. The patient's condition was normal during this pregnancy till about the thirtieth week when there was evidence of some excess of liquor amnii. He considered it expedient to puncture the membranes during labour. The fertility of this woman is striking in view of the fact that she was being treated with insulin and also the pregnancies do not appear to have adversely affected her diabetic condition.

Discussion. The PRESIDENT said it was interesting to hear of the successful outcome in this case. In discussing a previous paper by Dr. Tighe a gloomy prognosis for future pregnancies was predicted for this woman, by various speakers. It had now been proved that they were wrong. He asked if the pregnancy at the thirty-fourth week was a spontaneous one, or if labour was induced.

Dr. J. F. CUNNINGHAM asked Dr. Tighe how he had treated this patient during pregnancy. Diabetes was rather a new complication to meet in pregnancy, because formerly diabetic women were either sterile or else they miscarried. With the giving of insulin pregnancy had now been made possible for them. The amount of insulin that these patients took before pregnancy had very little bearing on the amount that they required during pregnancy. There was a great tendency during pregnancy for hyper-

glycaemia to develop. A number of these patients developed toxaemia either in the early months of pregnancy or in the latter months. Some of the infants of diabetic mothers were large, but a great many of them were not. Whether this was due to the toxaemia which was often found in these cases or not, it was very difficult to say. Some doctors believed that the infants died from hyperglycaemia. He did not think this was so.

Dr. G. C. DOCKERAY said that he had done a post-mortem examination on this patient's last baby. In women with diabetes there was a fall in sugar tolerance in the latter half of pregnancy, and a fall in the puerperium, and there was also a tendency to hyperglycaemia in the puerperium. He asked if there was any other explanatiton of the large size of the babies of diabetic women than that of hyperglycaemia in the mother. So far as he knew this view was at present merely conjecture.

Dr. TIGHE, in replying, said that the weight of the baby at the thirty-fourth week was 7 pounds. Labour was spontaneous. He thought that possibly the reason for this was the accompanying hydramnios. Delivery was spontaneous. Before pregnancy the woman had been in a general hospital where she had been told that the dose of insulin should not be increased, if possible, during pregnancy. He, however, had increased the dose from 75 units to 90 units per diem. In the general hospital she had been told to try to take a good deal of carbohydrate and keep her dose of insulin down. The cause of death of her previous baby was said to be renal apoplexy. This was, perhaps, due to the accompanying hyperglycaemia in the maternal circulation.

ROYAL ACADEMY OF MEDICINE IN IRELAND

FEBRUARY 1938

A meeting of the Royal Academy of Medicine in Ireland was held in the Royal College of Physicians on Friday, February 18th, 1938. The President, Dr. J. S. Quin, was in the chair.

Dr. F. W. DOYLE read

NOTES ON A CASE OF PUERPERAL ANAEMIA WITH PULMONARY INFARCTION.

The patient was a strong, healthy woman, aged 32 years. Her confinement was uncomplicated and her puerperium up to the twelfth day was normal, then pyrexia first occurred. Three separate pulmonary infarctions followed, on the fourteenth, twenty-second and twenty-seventh days, the first involving the left lung, and the others the back and front of right lung. Each infarction was associated with symptoms of acute distress, pain

and dyspnoea. A blood-count revealed 2 to 4 million red cells, haemoglobin 45 per cent, colour-index I, white cells 7,421. The relatively high colour-index with poikilocytosis, and anisocytosis with a complete absence of leucocystosis strongly suggested a severe or pernicious type of anaemia. Uterine culture and blood-culture were both negative. The treatment adopted was morphine, antiphlogistine locally, with collosol iodine, 8 grm., intravenously, this latter being given daily for three weeks. Comnadin, 2 c.c., intramuscularly was employed towards the end. Liver, iron, and hydrochloric acid were administered throughout. Subsequent blood examinations, at the fourth and eighth weeks of the puerperium, revealed a satisfactory response, and the patient finally left the nursing home with a comparatively normal blood-picture at the end of the tenth week.

The PRESIDENT said that he thought the condition was one of a low grade infection with possibly some focus of infection in the broad ligaments, or the deep veins of the leg which swelled, causing a discharge of emboli. He had no doubt that the good result which Dr. Doyle had achieved was due to the fact that he had treated the patient on purely symptomatic lines.

The Master of the Coombe Hospital, Dr. R. M. CORBET, referred to the fact that the blood-culture and the uterine swab had been sterile in this case, and said that he had had under his care in hospital some patients with pyrexia, some of whom had emboli, in whom the swabs were sterile, but when the uteri were evacuated large quantities of pus had come away. The explanation was, apparently, that the organism was one which grew only under anaerobic conditions. This, he thought, might have been a possible explanation of Dr. Doyle's case. His, Dr. Corbet's, cases had had the most profound anaemia; two of them had to have a blood transfusion in order to make them fit for the ordinary handling which was necessary.

Dr. DOYLE, in replying, said that he was not able to say for certain that this case was a genuine one of anaemia of pregnancy. He thought anaemia with pyrexia was a definite clinical entity. If in the present case there had been an infection, there should have been a leucocytosis, but the latter was absent.

The Master of the National Maternity Hospital, Dr. J. F. CUNNINGHAM, read a paper on

THE DIAGNOSIS AND TREATMENT OF HYDATIDIFORM MOLE.

Having referred to the usual signs and symptoms of molar pregnancy, he stressed the value of the Aschheim-Zondek test and of X-rays in the diagnosis. He found that at the National Maternity Hospital during the last four years the incidence of hydatidiform mode was one in 1,532, but pointed out that as many of his cases of mole were sent into the hospital from outside the real incidence must be much less. He then discussed the various methods of treatment which have been recommended for the condition, viz. (1) rapid dilatation of the cervix and emptying the uterus with the finger or ovum forceps; (2) vaginal hysterotomy; (3) abdominal hysterectomy; (4) abdominal hysterotomy. He then reported 10 cases of mole treated

by him at the National Maternity Hospital in the last four years. He treated all 10 cases by a modified Watson induction. In nine cases the uterus responded to the medical induction and expelled the mole with very little bleeding. In the case in which induction failed he performed total hysterectomy. This patient was in a very bad general condition and was aged 48 years. This method of treatment in its immediate results and also, so far as these cases are concerned, in its remote results had proved the most satisfactory he has tried. Eight of the cases have been followed and two remain under observation. In no case had chorion-epithelioma developed. Whether the absence of chorion-epithelioma from this series is in any way connected with the method of treatment, he did not venture to say, but is of the opinion that the absence of all trauma in the evacuation may play some part in the reducing the danger of metastases.

He then described the technique of induction. Ten grains of quinine sulphate are given at night, followed in the morning by one and a half to two ounces of castor oil. A few hours later 10 more grains of quinine are given, followed by an enema and a hot bath. Pituitary extract in doses of 5 units is then given half-hourly, the first dose being given simultaneously with the enema. The total amount is never allowed to exceed 30 units. Thymophysin has been used with equal success and he recommends pitocin in cases with toxic symptoms.

Dr. T. M. HEALY showed

A SPECIMEN OF PERFORATING MOLE.

The patient had had three previous pregnancies. The present one had ended in September last with the spontaneous evacuation of a mole at approximately the tenth week of gestation. After this she had had no treatment till she was sent from the country at the end of October, when Dr. Healy first saw her. She had had a blood-stained vaginal discharge almost continuously since passing the mole, but stated that she felt quite well. The uterus was soft, and about the size of an 8 weeks' pregnancy. On November 1st Dr. Healy curetted the uterus and obtained very little material. The Aschheim-Zondek reaction was positive. In 10 days' time a blood-stained discharge again appeared. The Aschheim-Zondek reaction was negative. A second curettage was done; no change took place in the symptoms or physical signs. On November 25th total hysterectomy and bilateral salpingo-oöphorectomy were performed. Dr. Healy said he would like to gain some information as to whether there were any possible means of knowing, in cases such as this, whether such a uterus would ultimately become malignant, and if there was any way of differentiating between a uterus such as this, which was apparently benign, and one which was the site of chorion-epithelioma. Two other cases which he had seen had behaved clinically in exactly the same way as this, and yet the growth was malignant in both. He did not know whether a pathologist would care to state emphatically on the result of the Aschheim-Zondek reaction whether the disease was or was not malignant. He thought that hysterectomy was justified in patients who had had a molar pregnancy and whose uteri did not involute. Munroe Kerr laid great stress on the word "tense" as applied

to the uterus in this condition. His own experience of moles had been, on the whole, satisfactory, and he had found this to be on the whole a safe sign. The smaller textbooks used the word "boggy" when describing this condition, and, he thought, gave students an entirely wrong impression. He asked Dr. Cunningham if he curetted the uterus 10 or 12 days after the evacuation of a mole and again two months later, or if he waited two months before the curettage.

Dr. EDWARD SOLOMONS showed

A SPECIMEN FROM A CASE OF MALIGNANT MOLE.

The patient, Mrs. B.S., aged 52 years, was admitted to Dr. Steeven's Hospital on September 25th, 1937, complaining of nausea and vomiting for five weeks, which at first she believed was due to pregnancy. She menstruated normally up to July 25th, 1937; slight bleeding occurred on the day before her admission to hospital. She had spasms of moderate pain in the lower abdomen and noticed she was passing very little urine. She also complained of an irritating cough for three weeks previous to admission, and stated that she had lost a considerable amount of weight during her illness.

On admission she was emaciated. She had a hectic flush, and the general appearance was that of a woman with a rapid wasting disease. There were sores on the lips and the tongue was dry and thickly coated. Examination of the abdomen revealed a soft mass rising out of the pelvis reaching to the umbilicus. Vaginal examination showed the mass to be a large soft uterus with the cervix closed. Ballottment was not obtained. With the exception of some crepitations at the bases of both lungs abnormality was not found in the respiratory or cardiac systems. The temperature was 92.4°F. and the pulse-rate 130. The blood-pressure was 142/72. The sedimentation rate of the blood was 40 minutes. The urine contained a few pus cells, a moderate number of red-blood cells, epithelial cells and plenty of hyaline and granular casts. The sputum was examined for tubercle bacilli but none were found. A radiograph of the uterus did not show any evidence of a foetus.

The urine was sent for a Aschheim-Zondek test; while awaiting the result the dehydration was treated with rectal salines. For two days the general condition was serious and the vomiting was very persistent, but on the third day she was able to take some peptonized milk without vomiting. The cough was troublesome and accompanied by fairly profuse expectoration. Five days after admission the patient spontaneously passed a large hydatidiform mole and, as bleeding continued, the uterus was explored and some large pieces of the mole were separated digitally and removed with ovum forceps; light curettage with Rheinstadter's curette completed the operation. Her convalescence was remarkable, for with the exception of a rise of temperature to 100°F. on the evening of passing of the mole, she improved in a most dramatic manner. Twelve days later she was discharged from hospital in excellent condition and told to return in four weeks' time. On discharge from the hospital, the urine was normal. The sedimentation rate

of the blood had risen to 1 hour and 10 minutes. The uterus was enlarged to about the size of a 3 months' pregnancy. The Zondek-Aschheim test was still positive and the Wasserman reaction negative.

On the 27th October 1937, that is, 4 weeks after the expulsion of the mole, the Zondek-Aschheim test was still positive. A diagnostic curettage was performed, the curettings from which were heavy. There was no evidence of malignancy by microscopic examination of the curettings as only remnants of degenerated chorionic villi and involuting and partly necrotic villi with chorionic wandering cells were found. In view of these results it was decided to temporize and to repeat the Zondek-Aschheim test and the diagnostic curettage in one month's time.

On the 1st November 1937 she was discharged, but 10 days later she commenced to have attacks of haemorrhage; on the 13th November she was re-admitted to hospital. As the uterus was still enlarged to about the size of a 3 months' pregnancy, total hysterectomy with removal of both tubes and ovaries was performed on the 17th November. Nothing abnormal was observed in the abdomen or pelvis at operation, but all the tissues were extremely soft and free bleeding occurred very easily. Having had an uneventful and speedy convalescence, the patient was discharged from hospital 2 weeks after operation feeling and looking well.

Dr. G. DOCKERAY, in describing the pathological findings, said that the uterus was slightly enlarged and full of blood-clot. He saw what he thought was a chorion-epithelioma attached to the wall of the uterus. Different textbooks used different names for this condition, but so long as one knew what one was dealing with, he did not think it really mattered what it was called. The condition had first been described in 1867, and had been called malignant mole, perforating mole, and mole intravenora, which he thought was the best name of all. Some of these moles grew right into the veins. If the tissue was so malignant it could grow back into the walls of the villi, and therefore no villi could be seen which had not been destroyed.

The PRESIDENT said that it was a long time since the Section had had before it a series of cases of such an extremely interesting clinical and pathological condition. The diagnosis of hydatidiform mole had become more easy since the advent of X-rays and the Aschheim-Zondek test. He referred to a case which he had seen many years ago which had been diagnosed as one of hydatidiform mole. Labour was induced by the insertion of tents into the cervical canal; when the cervix was sufficiently dilated to enable the uterine contents to be palpated, the doctor in charge of the case was rather downcast to feel foetal parts. The patient delivered herself of twins and a hydatidiform mole. It was interesting to note how frequently toxaemic complications were met with in these cases. With regard to the treatment outlined by Dr. Cunningham, he said that before the introduction of medicinal treatment in these cases one was always in doubt what to do. Munroe Kerr advocated vaginal hysterectomy, but the amount of haemorrhage which might follow this procedure gave rise to a certain amount of alarm. He had no doubt that in some cases hysterectomy was probably the simplest and the safest way of dealing with a patient, especially an elderly patient who had had children before.

The Master of the Rotunda Hospital, Dr A. H. DAVIDSON, said that at the Rotunda Hospital in 6 years there had been 14 cases of vesicular mole. Only 1 of the patients was a primigravida. Five out of the 14 were over 40 years of age, a fact which bore out what most observers said about the condition that it was a disease of later child-bearing life. Only 3 of the cases had been associated with toxaemia, although toxaemia was supposed to be common in association with vesicular mole. In 10 cases the uterus was bigger than it would be in normal pregnancy, in most cases twice as big, but in 4 cases it was smaller than in normal pregnancy. These 4 all passed the mole *per vaginam*, 3 of them spontaneously and the other after the induction of labour. It was possible that the mole was dead in the cases in which the uterus was smaller than in normal pregnancy and alive in the cases in which it was bigger. The history in all cases was of bleeding beforehand, and they were all treated by the introduction of tents. Chorion-epithelioma developed in 2 cases and a perforating mole in one. One of the greatest diagnostic difficulties was to differentiate between a vesicular mole and the type of uterus in which bleeding occurred about the fifth or sixth month. The foetal heart could not be seen by X-rays, and the Zondek-Aschheim test was very often indefinite. In cases of hydramnios the Aschheim-Zondek test was always positive. In the Rotunda Hospital cases of mole in which delivery was not spontaneous were treated by the insertion of tents.

The Master of the Coombe Hospital, Dr. R. M. CORBET, said that in all midwifery the more you let the patient do it for you the better you would be. This applied to moles almost more than to anything else. If you could induce a patient to evacuate a mole you would undoubtedly get the best result. When a mole was not spontaneously evacuated he used tents; in one case he had inserted a stomach tube into the mole, and the mole had been evacuated without undue bleeding. The amount of haemorrhage depended on the size and the liveliness of the mole. A comparatively small but very live mole might give much trouble. He had noticed on several occasions that about the time that the mole began to be evacuated the patient developed an extremely rapid pulse-rate, a rate quite out of proportion to the blood loss and which did not fall in at all with the general appearance of the patient. This type of pulse gave one the impression of being a toxic pulse rather than a haemorrhagic one. He said that in his opinion hysterectomy was justified in cases in which the Aschheim-Zondek reaction remained positive after malignant disease had been excluded by curettage of the uterus and when vaginal haemorrhage persisted. When it was impossible to eliminate chorion-epithelioma, it was necessary to act as if chorion-epithelioma had been diagnosed. It was necessary to operate on suspicion in these cases, and put up with the occasional cases in which subsequent pathological examination suggested that the operation was unnecessary.

Dr. O'DONEL BROWNE agreed with previous speakers that Dr. Cunningham was to be thanked for having advised the method of induction of labour in such cases of hydatidiform mole as those recorded, but suggested that this technique was not devoid of danger. He referred to the cases of the penetrating moles which had produced almost complete uterine rupture. He believed that large doses of oxytocics in such cases might promote violent

uterine contractions, the cervix being closed, and lead to complete rupture. This, of course, would be a major calamity because haemorrhage and dissemination of the growth would inevitably occur into the peritoneal cavity.

He asked Dr. Cunningham what method of treatment he adopted in moles which were actively bleeding; the cervix being closed. His opinion as to the advisability of hysterectomy in cases of suspected malignant mole was that we must perform blind hysterectomy in many cases as it was evident that the pathologist and biochemist were often unable to give a definite opinion.

From the clinical standpoint Dr. O'Donel Browne felt that it was unjustifiable to temporize in the presence of persistent sub-involution, repeated presence of chorionic elements in curettings or a positive Aschheim-Zondek test and advocated hysterectomy when such symptoms and findings were present. The suggestion that the moles in which the uterus was smaller than normal for the duration of the amenorrhoea were dead, and when the uterus was larger than normal the moles were alive was interesting.

In his experience he found that it was more difficult to induce labour in any case in which the ovum was dead and also disagreed with other speakers in his behalf that post-partum haemorrhage was more likely to occur following evacuation of a dead ovum from the uterus than when the ovum had been alive. In his experience toxaemias with molar pregnancy were not common, although albuminuria was often found.

He believed that this could be explained by the fact that shock frequently developed when blood was extravasated within the uterine cavity, and in support of his view said that no evidence of toxaemia existed in such cases other than the albuminuria.

Dr. A. W. SPAIN said that Dr. Cunningham had obtained very good results in the treatment of this condition. He had seen with Dr. Cunninham the case in which he had done a hysterectomy, and he thought that this treatmtent, in this particular case, was undoubtedly justified. As a general line of treatment, however, he thought it would be very unfortunate because many uteri would be unnecessarily sacrificed. The cases which were most likely to respond to treatment were those in which the mole was alive. When these moles were growing he thought there must be an excess of oestrin in the blood. He mentioned a case in which he had tried to induce labour by the administration of rather large doses of oestroform every six hours. After a few days a dead mole was evacuated with the help of Watson's method of induction. He thought it would be advisable in cases in which the onset to labour was delayed to give doses of oestroform for 5 or 6 days. It was sometimes very difficult to diagnose chorion-epithelioma. About a year ago he had seen a woman who had spontanously expelled a mole. Her doctor was quite satisfied that everything had come away. Three weeks later she began to bleed, and bled for 8 or 10 days, so her doctor sent her up to see him. The uterus was not really enlarged, and was not at all soft or boggy. He, Dr. Spain, curetted her uterus; no tissue was found which could be described as even suspicious of chorion epithelioma, yet the Zondek-Aschheim test was positive. After the curettage she did not bleed. In a fortnight's time the Zondek-Aschheim test was still positive. He did not know whether to remove the uterus or not, but he did not. It would have

been rather a tragedy if he had had to because the woman was only 21 and this was her first pregnancy. He did a Zondek-Aschheim test regularly for four months, and each time it was positive undiluted, negative in dilutions of 1 in 10 and 1 in 20. She was now very well and the Zondek-Aschheim reaction was negative. In cases of mole it was possible that if the blood was tested for hormones an excess of one particular hormone might be found. It would appear that parts of the tissue might remain in the wall of the uterus some time after the expulsion of the mole, and, possibly, so long as there were the Zondek-Aschheim test would remain positive.

Dr. F. W. BOYLE asked about the subsequent menstrual history of these cases. It would be interesting to know what was found in the ovaries after hysterectomy. In some cases the ovaries were converted into luteal cysts. Was amenorrhoea a common finding in these cases? He knew of one case in which there had been amenorrhoea for 12 months after the expulsion of a mole. He thought that this was due to the continuance of the luteal cysts in the ovary. He would like to know from Dr. Cunningham a little more about the question of curetting. Should it be done immediately after the evacuation of the mole or later? He thought that the time to do it was immediately after the mole had been evacuated.

Dr. D. HANLEY asked when the Zondek-Aschheim test became negative after a normal pregnancy.

Dr. Cunningham, in replying, said that he always curetted the uterus within 2 months after the evacuation of the mole. He did not think that there was any hurry about curettage in these cases. The Zondek-Aschheim reaction was very helpful, but it was wise not to place too much reliance on it. Some textbooks said that the Zondek-Aschheim test remained positive for 2 months after the expulsion of a mole without forming chorion-epithelioma. It was very hard to explain why toxaemia was so common in these cases. In one of these cases the uterus was septic. The patient was not examined for at least 2 months before the uterus was removed. Two of his patients with dead moles were primiparae; one of them was a woman aged 38. When he first saw her he thought the case was one of missed abortion.